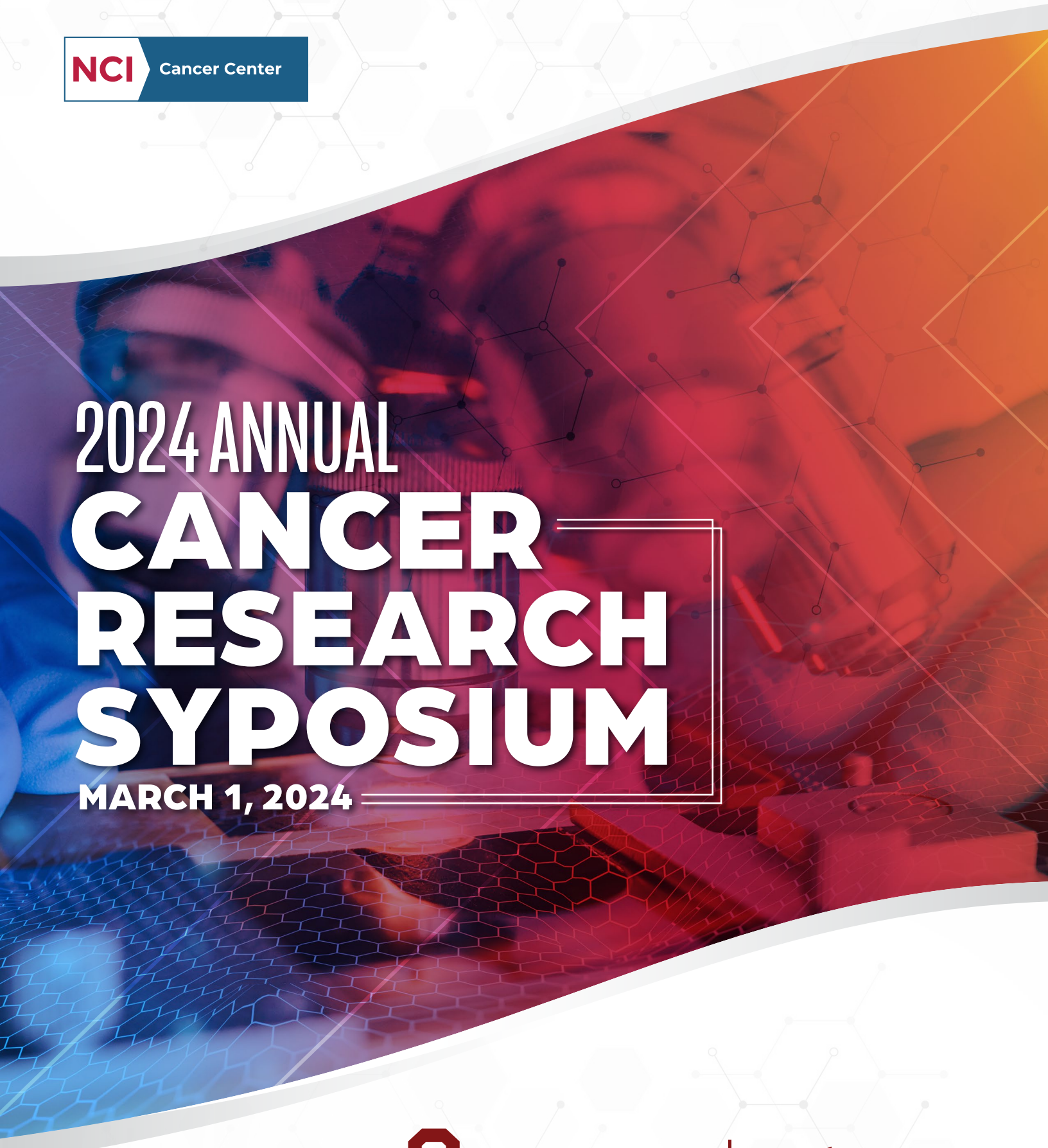
NCI Cancer Center



2024 ANNUAL CANCER RESEARCH SYPOSIUM

MARCH 1, 2024

OU Health | Stephenson Cancer Center

The UNIVERSITY *of* OKLAHOMA HEALTH SCIENCES

The Stephenson Cancer Center wishes to recognize and thank the Oklahoma Tobacco Settlement Endowment Trust (TSET) for co-sponsoring the 2024 Stephenson Cancer Research Symposium.

In 2012 TSET awarded a five-year, $30.25 million grant to the Stephenson Cancer Center to establish the Oklahoma TSET Cancer Research Program. In 2017 TSET renewed this award for an additional five year period and in 2022 for an additional three year period.

The mission of the Oklahoma TSET Cancer Research Program is to decrease the burden of cancer in Oklahoma and nationally through promoting, coordinating and supporting innovative cancer research. It seeks to accomplish this mission through:

- Attracting cancer researchers with grant funding from the National Cancer Institute and other national sponsors to Oklahoma
- Developing trans-disciplinary, collaborative cancer research programs
- Promoting inter-institutional partnerships to leverage unique strengths at research institutions in Oklahoma
- Enhancing research infrastructure and shared resources to enable and support innovative and nationally-competitive cancer research
- Serving as a statewide resource for researchers and institutions that conduct cancer research

The Oklahoma TSET Cancer Research Program supports a wide range of programs, shared resources and initiatives designed to accomplish these goals.

With support from the Oklahoma TSET Cancer Research Program the Stephenson Cancer Center accomplished the following:

- Increased cancer center membership from 56 to 319 members at nine academic institutions across Oklahoma
- Recruited seventy one new cancer researchers to Oklahoma
- Funded over fifty seed and directed-research grants to cancer investigators in Oklahoma
- Enhanced five Shared Resource facilities
- Hosted over 366 research seminar speakers
- Hosted annual statewide Cancer Research Symposium that bring together over 250 researchers from around the state
- Hosted over 125 undergraduate students from 34 different universities for summer cancer research experience.
- Since the inception of the TSET grant, the SCC has enrolled more than 8,000 patients to interventional clinical trials.

TSET Health Promotion Research Center

OU Health Stephenson Cancer Center
The UNIVERSITY of OKLAHOMA HEALTH SCIENCES

OU Health Stephenson Cancer Center wishes to recognize and thank the TSET Health Promotion Research Center (HPRC) for co-sponsoring the 2024 Annual Cancer Research Symposium

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The TSET Health Promotion Research Center (HPRC) is a leading research center that focuses on reducing the burden of disease in Oklahoma by addressing modifiable health risk factors such as tobacco use, sedentary lifestyle, poor diet, cancer screening, and risky alcohol and other substance use through research, novel intervention development, and dissemination of research findings.

The center was established in 2007 with funding from the Oklahoma Tobacco Settlement Endowment Trust (TSET) as part of their efforts to support statewide and community-based cessation and intervention projects.

The HPRC contains four major resources that facilitate research: the Mobile Health Shared Resource, the Tobacco Treatment Research Program, the Training Program, and the Tobacco Regulatory Science Clinical Laboratory.

HPRC Directors, Faculty

Michael Businelle, PhD (Director)
Darla Kendzor, PhD (Director)
Jamie Rhudy, PhD (Director, Tulsa)
Adam Alexander, PhD
Desiree Azizoddin, PsyD
Sarah Borengasser, PhD
Ashlea Braun, PhD
Than Bui, MD, DrPh
Meng Chen, PhD
Amy Cohn, PhD
Summer Frank-Pearce, PhD
Amanda Kong, PhD
Julia McQuoid, PhD
Jordan Neil, Ph.D.
Motolani Ogunsanya, PhD
Jason Oliver, PhD
Zachary Pope, PhD
Lurdes Queimado, MD, PhD
Michael Robertson, PhD
Katelynn Romm, PhD
Erin Vogel, PhD

TSET

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2024 Annual Cancer Research Symposium

9:00 – 10:00 am	**Trainee Feedback Panel Discussion** Samis Center Auditorium
10:00 – 11:00 am	**Registration & Poster Check-In** Samis Center Main Entrance
11:00 – 11:30 am	**State of the Cancer Center Address** Samis Center Auditorium
11:30 – 12:30 pm	**ACS-IRG Awardee Session** Samis Center Auditorium
12:30 – 2:00 pm	**Lunch & Poster Session** Lunch (Main Level); Posters (Level 1)
2:00 – 3:05 pm	**Immuno-Oncology Session I: Emerging Clinical/Translational Aspects of Immuno-Oncology** Samis Center Auditorium
	Health Promotion Research Center Session I: Tobacco Use/Cessation Samis Center Basement
3:05 – 3:20 pm	**Break**
3:20 – 4:25 pm	**Immuno-Oncology Session II: Utilizing Novel Omics & Computational Approaches in Immuno-Oncology** Samis Center Auditorium
	Health Promotion Research Center Session II: Cancer Disparities & Survivorship Samis Center Basement

OU Health | Stephenson Cancer Center
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2024 Annual Cancer Research Symposium

4:15 – 4:30 pm	**Break**
4:30 – 4:50 pm	**Awards/Closing Remarks** Samis Center Auditorium
5:00 – 6:00 pm	**Reception** Samis Center Level 1

OU Health | Stephenson Cancer Center
The UNIVERSITY of OKLAHOMA HEALTH SCIENCES

2024 Annual Cancer Research Symposium

9:00 – 10:00 am

Trainee Feedback Panel Discussion
Samis Center Auditorium
Rajagopal Ramesh, PhD
Associate Director, Cancer Research Training & Education Coordination
Joan Walker, MD
Associate Director, Belonging & Inclusion
Adam Alexander, PhD
Assistant Director, Belonging & Inclusion

10:00 – 11:00 am

Registration & Poster Check-In
Samis Center Main Entrance

11:00 – 11:30 am

State of the Cancer Center Address
Samis Center Auditorium
Robert Mannel, MD
Director, OU Health Stephenson Cancer Center

11:30 – 12:30 pm

ACS-IRG Awardee Session
Samis Center Auditorium
Moderators: Rajagopal Ramesh &

Intracerebral Doxorubicin Delivery via a Nanocomposite Hydrogel Depot is Safe and Reduces Tumor Volume in Mouse Xenograft Model of Glioblastoma
John Clegg, PhD

Investigating the Metabolic Vulnerability of Bladder Cancer for Intercepting Its Progression
Venkateshwar Madka, PhD

Elucidating Multilevel Influences on Tobacco Use at the Intersection of Sexual Orientation and Rurality
Katelyn Romm, PhD

Novel Optical Imaging Platform for Early Cancer Detection
Qinggong Tang, PhD

OU Health | Stephenson Cancer Center
The UNIVERSITY of OKLAHOMA HEALTH SCIENCES

2024 Annual Cancer Research Symposium

12:30 – 2:00 pm

Lunch & Poster Session
Lunch (Main Level); Posters (Level 1)

2:00 – 3:05 pm

Immuno-Oncology Session I:
Emerging Clinical/Translational Aspects of Immuno-Oncology
Samis Center Auditorium
Moderators: Susanna Ulahannan & Rafeh Naqash

Emerging Clinical and Biomarker Insights for Immune Toxicity Due to Checkpoint Inhibitors Abdul Rafeh Naqash, MD

Cardio-Oncology and the Intersection of Immunotherapy - Lessons Learned
Zain Asad, MD

The Intersection of Radiation and Immunotherapy: Updates for the S1933 Trial Raid Aljumaily, MD

Exploring Systemic Treatment Approaches for Advanced Pure Large Cell Neuroendocrine Carcinoma (LCNCE): A Multicenter Retrospective Analysis
Unaiza Zaman, MD

Immunotherapy Outcomes in Patients of Native American Ethnicity: A Multicenter Retrospective Study
Mihn Phan, MD

Panel Discussion & Session Q & A

Health Promotion Research Center Session I:
Tobacco Use/Cessation
Samis Center Basement
Moderator: Darla Kendzor

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2024 Annual Cancer Research Symposium

Measuring DNA Damage to Evaluate Electronic Cigarette Use as a Tobacco Harm
Vengatesh Ganapathy, PhD

Machine Learning Predictions of Smoking Trends: Insights from the PATH Study
Hanxia Li, PhD

Empowering Our Community, Reclaiming Our Health: Developing a Community-engaged Smoking Cessation Pilot Intervention for Sexual and/or Gender Minoritized People in Oklahoma
Julia McQuoid, PhD & Taylor Raye

3:05 – 3:20 pm **Break**

3:20 – 4:25 pm **Immuno-Oncology Session II: Utilizing Novel Omics & Computational Approaches in Immuno-Oncology**
Samis Center Auditorium
Moderators: Wei Chen & Adam Asch

Single-cell RNA-sequencing Analysis Reveals the Remodeling of Breast Tumor-infiltrating Lymphocytes Treated with Localized Ablative Immunotherapy
Kaili Liu, PhD

Multi-omic Analysis Unravels the Prognostic and Predictive Value of LAG3 Expression in Urothelial Carcinoma
Adanma Ayanambakkam, MD

Honing in on Spatial Transcriptomics to Evaluate the Tumor Microenvironment
Tae Gyu Oh, PhD

Detecting Neoepitope-specific Immune Response and TCR Repertoire Diversity
Marmar Moussa, PhD

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2024 Annual Cancer Research Symposium

Panel Discussion & Session Q & A

Health Promotion Research Center Session II: Cancer Disparities & Survivorship
Samis Center Basement
Moderator: Elizabeth Hile

Disparities in Primary and Secondary Breast Cancers Among Women in Oklahoma
Amanda Janitz, PhD, MPH, BSN

Preliminary Feasibility and Acceptability of an Interdisciplinary, Single-session, Telehealth Class for Patients with Cancer-related Pain
Desiree Hilton Azizoddin, PsyD

Feasibility of Wearable Focal Vibration for Chemotherapy-induced Peripheral Neuropathy: Interim Results
Josiah Rippetoe, PhD

Impact of Tobacco Smoke Exposure on Cisplatin Efficacy in Head and Neck Cancer
Balaji Sadhasivam, PhD

4:15 – 4:30 pm **Break**

4:30 – 4:50 pm **Awards/Closing Remarks**
Samis Center Auditorium

5:00 – 6:00 pm **Reception**
Samis Center Level 1

OU Health | Stephenson Cancer Center
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TRAINEE FEEDBACK DISCUSSION PANEL

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STATE OF THE CANER CENTER

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ACS–IRG AWARDEES

ACS-IRG Awardee Session

Samis Center Auditorium

11:30 – 12:30 PM **ACS-IRG AWARDEE SESSION**

Moderators: Rajagopal Ramesh &

11:30 – 11:45 AM **Intracerebral Doxorubicin Delivery via a Nanocomposite Hydrogel Depot is Safe and Reduces Tumor Volume in Mouse Xenograft Model Glioblastoma**

John Clegg
Assistant Professor
Stephenson School of Biomedical Engineering
University of Oklahoma

11:45 – 12:00 PM **Investigating the Metabolic Vulnerability of Bladder Cancer for Intercepting its Progression**

Venkateshwar Madka
Assistant Professor
Department of Internal Medicine
University of Oklahoma Health Sciences

12:00 – 12:15 PM **Elucidating Multilevel Influences on Tobacco Use at the Intersection of Sexual Orientation and Rurality**

Katelyn Romm
Assistant Professor
Department of Family and Preventive Medicine
University of Oklahoma Health Sciences

12:15 – 12:30 PM **Novel Optical Imaging Platform for Early Cancer Detection**

Qinggong Tang
Assistant Professor
Stephenson School of Biomedical Engineering
University of Oklahoma

INTRACEREBRAL DOXORUBICIN DELIVERY VIA A NANOCOMPOSITE HYDROGEL DEPOT IS SAFE AND REDUCES TUMOR VOLUME IN MOUSE XENOGRAFT MODEL OF GLIOBLASTOMA

John R. Clegg[1,2,3,4*], Mulan Tang[1], Christopher Pierce[1], Hunter Helvey[1], Bradley Sanchez[1], Hannah Homburg[5], James Battiste[2,5]

[1] Stephenson School of Biomedical Engineering, OU Norman; [2] Stephenson Cancer Center, OU Health Sciences Center; [3] Harold Hamm Diabetes Center, OU Health Sciences Center; [4] Institute for Biomedical Engineering, Science, and Technology, OU Norman; [5] Department of Neurosurgery, OU Health Sciences Center

**clegg@ou.edu*

Abstract: Glioblastoma (global prevalence = 300,000 cases per year) is an especially deadly form of brain cancer, with an average survival of 15-18 months and a 5-year survival rate of only 7%. Glioblastoma treatment is challenging, relative to treatment for other solid tumors, as neurosurgeons and neurooncologists must minimize both the resected tumor margin and the brain tissue volume exposed to therapeutic radiation post-surgery. The chemotherapeutic regimens indicated for glioblastoma are also lacking. Our long-term goal is to develop a drug delivery device that enables intracerebral chemotherapy, with the desired tissue penetration depth of 3 cm (relative to the tumor margin). Here, we developed a modular nanocomposite hydrogel for intracerebral chemotherapy, using doxorubicin as a model chemotherapeutic agent. Hydrogels were synthesized from chemically-modified brain extracellular matrix-mimicking polymers and doxorubicin-loaded biodegradable poly(lactic-co-glycolic acid) nanoparticles, which were dispersed in sterile saline and crosslinked into a network using 365 nm light. The formed hydrogel was injectable and has a compressive stiffness similar to native brain tissue (~1 kPa). Intracerebral injection of 10 microliters of hydrogel was well tolerated in both healthy mice and mice bearing G55 brain tumor xenografts. Due to the sustained release profile of doxorubicin from the nanocomposite hydrogel, relative to a bolus dose of doxorubicin in saline, we were able to safely deliver more than three times more doxorubicin (100 μg) intracerebrally than what was previously reported in the literature (30 μg). Athymic mice bearing G55 tumors that received our novel intracerebral injection had smaller tumor volumes at 7- and 14-days post-treatment, relative to untreated tumor-bearing mice and tumor-bearing mice that received less than 30 μg of doxorubicin. We are currently completing a survival study, which compares the extent to which intracerebral doxorubicin (100 μg in nanocomposite gel) extends mouse survival (G55 model) relative to saline, gel alone, and standard-of-care treatment (IV temozolomide). Taken together, our data indicate that doxorubicin-loaded nanocomposite hydrogels can be safely injected intracerebrally in a live animal and reduce glioblastoma tumor burden. Future studies need to evaluate the extent to which hydrogel-mediated drug delivery enables deep brain penetration of the encapsulated therapeutic, as well as compare therapeutic outcomes for intracerebral doxorubicin-hydrogel to standard-of-care treatments.

Funding acknowledgement: This work was supported by Institutional Research Grant number IRG-19142-01 from the American Cancer Society

INVESTIGATING THE METABOLIC VULNERABILITY OF BLADDER CANCER FOR INTERCEPTING ITS PROGRESSION.

Venkateshwar Madka

Center for Cancer Prevention and Drug Development, Stephenson Cancer Center, Hem-Onc Section, Department of Medicine, University of Oklahoma HSC.

Bladder cancer (BC) is a common malignancy of the urinary tract, and with significant mortality due to metastatic nature. Despite significant advances in diagnosis and treatment, the prevalence of BC continues to rise in both developing and developed countries. BC is characterized by the frequent recurrence of tumors following surgical resection and their progression to invasive disease. Hence there is an urgent need to develop novel and effective agents targeting the molecular mechanism adapted by BC to recur and spread locally and to distant sites. Metabolic reprogramming is one of the inherent cancer hallmarks, enhanced by different metabolic signaling pathways in cancer. Metabolic adaptations facilitate cancer initiation, proliferation, survival, invasion, and metastasis. Aerobic glycolysis (the Warburg effect) has long been considered a dominant form of energy metabolism in cancer cells and emerging evidence indicates that other metabolic forms may play a critical role in many types of cancer. Thus, cancer metabolism has aroused immense interest recently and exploring this further will help to simultaneously explain the process of carcinogenesis and guide therapy. In recent years, the understanding of bladder cancer pathogenesis at the molecular level has evolved rapidly, allowing for the identification of promising signaling pathways that contribute to disease development and, thus, enabling exploration of novel agents for intercepting its progression. Data from our lab and others indicate that bladder tumors have dysregulated galactose metabolism suggesting that tumor cells may be dependent on this pathway, and it could be critical for their survival. We have identified significantly overexpressed enzymes in BC whose expression strongly correlates with tumor grade and survival of the patients. Using suitable preclinical models, we are studying the effects of genetic and pharmacological inhibition of this novel target on BC cells survival and therapeutic response. (Supported in part by Institutional Research Grant number 134128-IRG-19-142-01 from the American Cancer Society).

ELUCIDATING MULTILEVEL INFLUENCES ON TOBACCO USE AT THE INTERSECTION OF SEXUAL ORIENTATION AND RURALITY

Authors: Katelyn F. Romm,[1,2] Clark Gilford Jr.,[1] Erin A. Vogel,[1,2] Julia McQuoid,[1,3] Meng Chen,[1,2] & Amy M. Cohn[1,2]

[1]TSET Health Promotion Research Center, Stephenson Cancer Center, Univeristy of Oklahoma Health Sciences Center, Oklahoma City, OK, USA

[2]Department of Pediatrics, College of Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA

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Background: Elevated tobacco use rates among sexual minority (SM vs. heterosexual)-identifying young adults (YAs) are well-documented, and partially driven by experiences of SM stress (e.g., negative social exchanges, discrimination). Unfortunately, this research has historically focused on SMYAs residing in urban contexts, despite greater tobacco use, tobacco-related disease, and community stigma toward SM individuals in rural communities. Research is needed to identify mechanisms contributing to tobacco use disparities among SMYAs residing in rural versus urban contexts to inform culturally-congruent tobacco cessation efforts.
Methods: We analyzed data from 330 female SMYAs (M_{age}=21.60, SD=2.22; 40.2% rural; 40.5% racial/ethnic minority) and 159 male SMYAs (M_{age}=22.14; SD=1.97; 36.4% rural; 51.6% racial/ethnic minority) from Oklahoma and surrounding states who completed an online survey in Fall 2023/Spring 2024. We conducted 3 sets of multivariable regressions among female and male SMYAs, separately, to identify associations between: 1) rural/urban residence and tobacco use outcomes (any past-month use of cigarettes, e-cigarettes, cigars, oral nicotine pouches, polytobacco use [use of 2+ products], nicotine dependence severity); 2) rural/urban residence and minority stress factors (mental health symptoms, current parental support, parental psychological control, peer support, discrimination, community safety, time spent in SM places); and 3) minority stress factors and tobacco use outcomes. Analyses controlled for age, race and ethnicity, and education level.
Results: Among female SMYAs, rural (vs. urban) residence was associated with multiple tobacco outcomes (i.e., higher odds of cigarette, nicotine pouch, and polytobcco use; greater nicotine dependence severity) and minority stress factors (i.e., mental health symptoms, lower parental support, greater psychological control, lower community safety, less time spent in SM places). Lower parental support and greater psychological control were in turn associated with higher odds of tobacco use (i.e., cigarette, nicotine pounch, polytobacco use) and greater nicotine dependence severity. Among male SMYAs, rural residence was not associated with tobacco use outcomes or minority stress factors and minority stress was not associated with tobacco use.

Conclusions: Female SMYAs residing in rural contexts report higher levels of multiple minority stress experiences, including mental health symptoms, negative parenting, and less community support. Negative parenting, in particular, may drive disparities in current cigarette and nicotine pouch use, as well as potentially problematic tobacco use (i.e., polytobacco use, nicotine dependence). Rural context was unrelated to minority stress and tobacco use among male SMYAs. Findings may highlight the need for tobacco cessation efforts to target female SMYAs residing in rural communities and to incorporate coping with negative impacts of experiences from parents. Findings also stress the need for larger-scale interventions that attend to community stigma with likely influences on parental treatment of SMYAs.

Acknowledgement of Funding: This work was supported by Institutional Research Grant number 134128-IRG-19-142-01 from the American Cancer Society. Drs. Romm, Vogel, McQuoid, Chen, and Cohn are also supported by Oklahoma Tobacco Settlement Endowment Trust (TSET) contract #R22-03 and the National Cancer Institute grant awarded to the Stephenson Cancer Center (P30CA225520).

NOVEL OPTICAL IMAGING PLATFORM FOR EARLY CANCER DETECTION

Qinggong Tang

Early and accurate detection of early neoplastic tissue remains a critical challenge in cancer diagnosis and treatment. Optical coherence tomography (OCT) is a novel high-resolution biomedical imaging technique for subsurface tissue imaging; however, it is less sensitive to detecting biochemical or molecular processes associated with early neoplastic formation before the exhibition of structural alterations. Fluorescence imaging has high sensitivity for detecting biochemical and molecular alterations, but has limited specificity. Combining these two complementary imaging technologies would improve the diagnostic capability for early cancer detection. My lab has developed novel multi-modal mesoscopic imaging technologies for subsurface imaging of tissue samples with high image resolution (<20 μm) and a penetration depth of several millimeters, comparable to the size of a standard punch biopsy. Furthermore, deep learning-based computer-aided diagnosis (DL-CAD) system is developed for automatically detecting and recognizing the tissue structures. In this talk, we will introduce these novel imaging platforms and their applications in early cancer detection.

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IMMUNO-ONCOLOGY

Immuno-Oncology Track

Samis Center Auditorium

2:00 – 3:05 PM

SESSION I: Emerging Clinical/Translational Aspects of Immuno-Oncology

Moderators: Susanna Ulahannan & Rafeh Naqash

2:05 – 2:15 PM

Emerging Clinical and Biomarker Insights for Immune Toxicity Due to Checkpoint Inhibitors

Abdul Rafeh Naqash
Assistant Professor
Department of Internal Medicine, Section of Hematology Oncology
University of Oklahoma Health Sciences

2:15 – 2:25 PM

Cardio-Oncology and the Intersection of Immunotherapy – Lessons Learned

Zain Asad
Assistant Professor
Department of Internal Medicine, Section of Cardiovascular Diseases
University of Oklahoma Health Sciences

2:25 – 2:35 PM

The Intersection of Radiation and Immunotherapy: Updates for the S1933 Trial

Raid Aljumaily
Associate Professor
Department of Internal Medicine, Section of Hematology Oncology
University of Oklahoma Health Sciences

2:35 – 2:45 PM

Exploring Systemic Treatment Approaches for Advanced Pure Large Cell Neuroendocrine Carcinoma (LCNCE): A Multicenter Retrospective Analysis

Unaiza Zaman
PGY5 Fellow
Department of Internal Medicine, Section of Hematology Oncology, Fellowship Program University of Oklahoma Health Sciences

2:45 – 2:55 PM

Immunotherapy Outcomes in Patients of Native American Ethnicity: A Multicenter Retrospective Study

Minh Phan
Assistant Professor
Department of Internal Medicine, Section of Hematology Oncology
University of Oklahoma Health Sciences

3:15 – 3:35 PM

Panel Discussion and Session Q & A

3:20 – 4:25 PM

SESSION II: Utilizing Novel Omics & Computational Approaches in Immuno-Oncology

Moderators: Wei Chen & Adam Asch

3:25 – 3:37 PM

Single-cell RNA-sequencing Analysis Reveals the Remodeling of Breast Tumor-infiltrating Lymphocytes Treated with Localized Ablative Immunotherapy

Kaili Liu
Research Assistant Professor
Stephenson School of Biomedical Engineering
University of Oklahoma

3:37 – 3:49 PM

Multi-omic Analysis Unravels the Prognostic and Predictive Value of LAG3 Expression in Urothelial Carcinoma

Adanma Ayanambakkam
Assistant Professor
Department of Internal Medicine, Section of Hematology Oncology
University of Oklahoma Health Sciences

3:49 – 4:01 PM

Honing in on Spatial Transcriptomics to Evaluate the Tumor Microenvironment

Tae Gyu Oh
Assistant Professor
Department of Oncology Sciences
University of Oklahoma Health Sciences

4:01 – 4:13 PM

Detecting Neoepitope-specific Immune Response and TCR Repertoire Diversity

Marmar Moussa
Assistant Professor
School of Computer Science
University of Oklahoma

4:13 – 4:25 PM

Panel Discussion and Session Q & A

EMERGING CLINICAL AND BIOMARKER INSIGHTS FOR IMMUNE TOXICITY DUE TO CHECKPOINT INHIBITORS

Abdul Rafeh Naqash, MD
Department of Internal Medicine, Section of Hematology Oncology
OU Health Sciences, OU Health Stephenson Cancer Center

Purpose: Recent evidence has shown that higher tumor mutational burden strongly correlates with an increased risk of immune-related adverse events (irAEs). By employing an integrated multi-omics approach, we further studied the association between relevant tumor immune microenvironment (TIME) features and irAEs.

Patients and Methods: Leveraging the U.S. Food and Drug Administration Adverse Event Reporting System (FAERS), we extracted cases of suspected irAEs to calculate the reporting odds ratios (RORs) of irAEs for cancers treated with immune checkpoint inhibitors (ICIs). TIME features for 32 cancer types were calculated based on The Cancer Genomic Atlas (TCGA) cohorts and indirectly correlated with each cancer's ROR for irAEs. A separate ICI-treated cohort of non-small cell lung cancer (NSCLC) was used to evaluate the correlation between tissue-based immune markers (CD8+, PD-1/L1+, FOXP3+, tumor-infiltrating lymphocytes [TIL]) and irAE occurrence.

Results: The analysis of 32 cancers and 33 TIME features demonstrated a significant association between irAEs RORs and the median number of base insertions and deletions (INDEL) neoantigens ($r = 0.72$), single nucleotide variant neoantigens ($r = 0.67$), and CD8+ T-cell fraction ($r = 0.51$). A bivariate model using the median number of INDEL neoantigens and CD8 T-cell fraction had the highest accuracy in predicting RORs (adjusted $r^2 = 0.52$, $p = 0.002$). Immuno-profile assessment of 156 NSCLC patients revealed a strong trend for higher baseline median CD8+ T cells within patients' tumors who experienced any grade irAEs. Using machine learning, an expanded ICI-treated NSCLC cohort (n = 378) further showed a treatment duration-independent association of an increased proportion of high-TIL (>median) in patients with irAEs (59.7% vs. 44%, $p = 0.005$). This was confirmed by employing the Fine-Gray competing risk approach, demonstrating higher baseline TIL density (> median) associated with a higher cumulative incidence of irAEs ($p = 0.028$)

Conclusion: Our findings highlight a potential role for TIME features, specifically INDEL neoantigens and baseline-immune infiltration, in enabling optimal irAE risk stratification of patients.

Exploring Systemic Treatment Approaches for Advanced Pure Large Cell Neuroendocrine Carcinoma (LCNEC): A Multicenter Retrospective Analysis.

Amin Nassar, Unaiza Zaman, Kelsey Matteson, Fatemeh Ardeshir, Jhanelle E. Gray, Javier Baena Espinar, David Kwiatkowski, Frank Aboubakar Nana, Christian Grohe, Fabrizio Citarella, Danny Pancirer, Justin Matthew Cheung, Alexander S Watson, Arthi Sridhar, Fionnuala Crowley, David Kaldas, Chul Kim, Kamya Sankar, Nichola Awosika, Abdul Rafeh Naqash, Anne C. Chiang; Yale Cancer Center, New Haven, CT; Yale New Haven Hospital, New Haven, CT; Emory, Atlanta, GA; Moffitt Cancer Center, Tampa, FL; Hospital Universitario 12 De Octubre, Madrid, Spain; Brigham and Women's Hospital, Boston, MA; Cliniques Universitaires Saint-Luc, Bruxelles, Belgium; Klinik für Pneumologie - Evangelische Lungenklinik Berlin Buch, Berlin, Germany; Bio-Medico Campus University Hospital, Roma, Italy; Stanford, Palo Alto, CA; Massachusetts General Hospital, Boston, MA; University of Colorado Cancer Center, Aurora, CO; Mayo Clinic, Rochester, MN; Mount Sinai, New York, NY; University of South Florida, Tampa, FL; Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC; 8700 Beverly Blvd, LOS Angeles, CA; Imperial College, London, United Kingdom; Medical Oncology/ TSET Phase 1 Program, Stephenson Cancer Center, University of Oklahoma, Oklahoma City, OK; Yale School of Medicine, New Haven, CT

Background:

Due to lack of prospective data, the optimal first line treatment approach for patients (pts) with pure LCNEC histology remains uncertain.

Methods:

Across 17 centers, we conducted a retrospective analysis of metastatic pure LCNEC (diagnosed at local institutions) who received 1st-line systemic therapy between 2015-2023. Pts were either treated with chemotherapy (chemo), immunotherapy (IO), or a combination (chemoIO). Clinical outcomes were progression-free survival (PFS), overall survival (OS), objective response rates (ORR), and treatment-related adverse events (trAE) as defined using CTCAE 5.0. Survival analysis by genomic alteration status (*TP53, RB1, STK11, KEAP1, KRAS*) and PD-L1 status were performed.

Results:

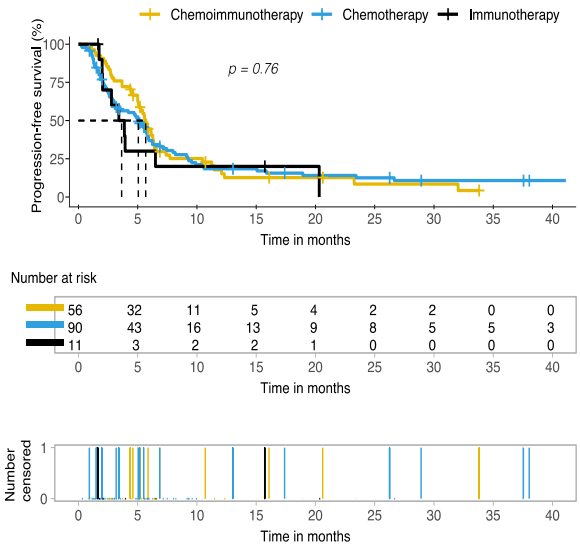
We identified 161 pts with median age of 67 years (IQR: 58-83) at 1st line systemic therapy; 54% (n = 87) were males. Median follow-up was 55 months (mo), 62 mo, and 29 mo for the chemo, IO, and chemoIO groups, respectively. 79% (n = 127) were former or current smokers. 1st-line treatments were chemo (n = 94), IO (n = 11), or chemoIO (n = 56). Of 85 pts with PD-L1 status, 58 (68%) were 0% and 27 (32%) were ≥1%. The most common chemo regimen was platinum-etoposide (n = 72, 78%). ChemoIO regimens included carboplatin/etoposide/atezolizumab (n = 23, 43%) and carboplatin/pemetrexed/pembrolizumab (n = 17, 31%). In the IO group, 1 patient received dual

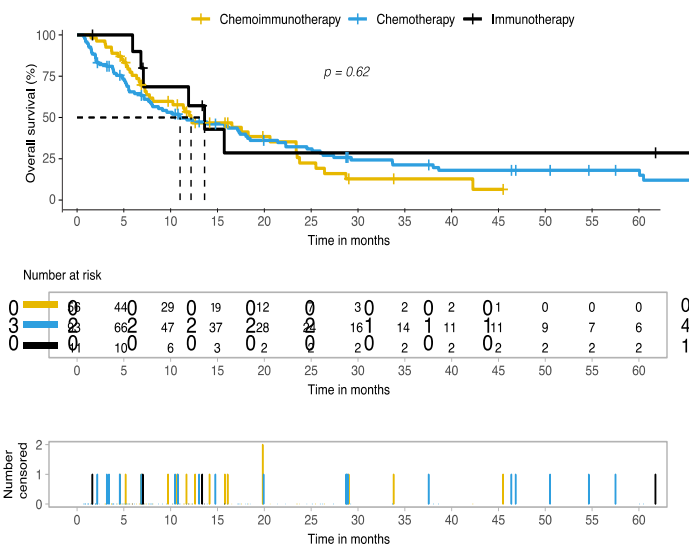
IO. Lung (n = 74, 46%) and liver (n = 71, 41%) were the most common sites of metastasisThere was no significant difference in PFS across the groups (median PFS [mPFS] chemoIO: 5.7 mo, 95% CI: 5.0-6.3, chemo: 5.1 mo, 95% CI: 3.1-5.9; IO: 3.6 mo, 95% CI: 1.7-6.5) on multivariable analysis adjusting for ECOG and "M" stage (p = 0.2 and 0.24 for chemoIO-chemo and chemoIO-IO comparisons, respectively). There was no difference in OS (mOS chemo: 11 mo, 95% CI: 7.6-17.4; IO: 13.6 mo, 95% CI: 5.9-not reached; chemoIO: 12.2 mo, 95% CI: 7.4-20.6, p = 0.5 and 0.8 for chemoIO-chemo and chemoIO-IO comparisons, respectively). ORR was 35.2% (31/88) in chemo, 25% (2/8) in IO, and 35.7% (20/56) in chemoIO (*p*= 0.46). There were no significant differences in PFS and OS outcomes by treatment group when divided by genetic profile (n = 79, methods), or by PD-L1 status (0% vs ≥1%). Any grade trAE occurred in 48 (51%), 5 (45%), and 28 (50%) pts treated with chemo, IO, and chemoIO, respectively. Grade ≥3 toxicity profiles are shown (table).

Conclusions:

For 1st-line treatment of LCNEC, similar PFS, OS, and ORR were seen for chemo, IO, and chemoIO. This questions the added benefit of chemoIO compared to chemo alone, and warrants future clinical trials to discern the optimal 1st line treatment.

Grade ≥3 (n,%)	Chemo	IO	ChemoIO
Any trAE	22 (23)	0 (0)	10 (18)
Fatigue	6 (6.4)	0 (0)	2 (3.6)
Anemia/thrombocytopenia	6 (6.4)	0 (0)	4 (7.1)
Nausea/vomiting	2 (2.1)	0 (0)	1 (1.8)
Diarrhea	3 (3.3)	0 (0)	0 (0)
Steroids	2 (2.1)	1 (9.1)	6 (11)
Discontinued due to toxicity	12 (23)	1 (17)	6 (11)


Chemoimmunotherapy
Chemotherapy
Immunotherapy
Progression-free survival (%)
p = 0.76
Time in months
Number at risk
56 32 11 5 4 2 2 0 0
90 43 16 13 9 8 5 5 3
11 3 2 2 1 0 0 0 0
Number censored
Time in months


Chemoimmunotherapy
Chemotherapy
Immunotherapy
Overall survival (%)
p = 0.62
Time in months
Number at risk
Number censored
Time in months

IMMUNOTHERAPY OUTCOMES IN PATIENTS OF NATIVE AMERICAN ETHNICITY: A MULTICENTER RETROSPECTIVE STUDY

Minh Phan

Introduction: Epidemiological data indicate that Native American (NA) patients (pts) with cancer may have worse outcomes vs. Caucasian American patients, despite receiving identical standard-of-care cancer treatments. Immune checkpoint inhibitors (ICI) have revolutionized the treatment of certain tumors; however, a uniform distribution of ethnicities is often not included in practice-changing ICI trials, especially documenting participation from the NA population.
Methods: This is a multi-center retrospective study from five tertiary care academic cancer centers that serve a high volume of NA pts the U.S. We included pts with a self-reported ethnicity as NA in the electronic medical records. We evaluated clinical outcomes and Immune-related adverse events (irAEs) of 98 NA pts age ≥18 years with various solid tumors treated with ICI monotherapy or in combination with other anti-neoplastic agents between 2015 to 2021. IrAEs were defined based on the Common Terminology Criteria for Adverse Events (version 5.0). Self-reported investigator assessment or RECIST 1.1. if available, was used to determine overall response rate (partial response + complete response).
Results: In the entire cohort of 98 patients, median age (range) at ICI initiation was 63 (24 -85) years, 54 (55%) were males, with 43 (44%) females and 1 unreported for gender. 77 (79%) of pts had ECOG performance status 0-1, 18 (18%) with ECOG ≥2 and 3 unknown; distribution of tumors (number [%]): non-small cell lung cancer (NSCLC) 32 (33%), renal cell carcinoma (RCC) 18 (18%), gynecological malignancies 9 (9%), small cell lung cancer (SCLC) 7 (7%), melanoma 7 (7%), Hepatocellular carcinoma and head/neck squamous cell carcinoma had 4 (6%) each, colon cancer, carcinoma of unknown primary, breast, and rectal cancer were 2 (2%) each. Most patients (57 [58%]) were treated with single agent ICI, 10 (10%) had dual ICI, 20 (20%) had chemotherapy plus ICI, and remaining had ICI plus tyrosine kinase inhibitor or ICI in a clinical trial/study drug. Most pts with stage IV NSCLC (79%) underwent next-generation sequencing evaluation of their tumor.
In the entire cohort of 98 patients, 21% had any grade irAE, 4 (6%) were reported to be grade (G) 3 or higher. The median time to irAE onset was 16 weeks and 5 patients discontinued ICI due to irAEs.
Clinical outcomes for the two most common histologic subgroups with stage IV disease (NSCLC and RCC) were assessed; In patients with stage IV NSCLC, the median PFS was 6.5 months (95%CI: 2.0-11.0), and the median OS was 14.8 months (95%CI: 5.0-23.0). Among patients with stage IV RCC, the median PFS was 5.5 months (95%CI: 3.0-11.0), and the median OS was 15.0 months (95%CI: 5.0-25.0).

Conclusion: Although limited by sample size, our emerging data provide a unique insight into ICI efficacy and irAEs in NA pts that have been unknown to date. To our knowledge, this is the first and only attempt to date aimed at evaluating ICI outcomes and tumor genomics in NA pts through a multicenter dataset through an ongoing collaboration. Further research is needed to fully characterize the efficacy and safety of ICI in NAs, including exploration of larger populations encompassing diverse malignancies and patients from additional tribes, a more in-depth characterization of tumor characteristics, including mutations and PD-L1 status, and comparative analyses with non-NA cancer patients.

SINGLE-CELL RNA-SEQUENCING ANALYSIS REVEALS THE REMODELING OF BREAST TUMOR INFILTRATING LYMPHOCYTES TREATED WITH LOCALIZED ABLATIVE IMMUNOTHERAPY

Kaili Liu[1], Ashley R. Hoover[1], Jacob Adams[1], Trisha I. Valero[1], Coline Furrer[1], Yuanhong Sun[1], and Wei R. Chen[1]*

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Lymphocytes, encompassing B and T cells, are crucial in antitumor immune responses, yet their activation pathways following localized ablative immunotherapy (LAIT) are not fully understood. We applied LAIT, integrating photothermal therapy (PTT) with intratumoral administration of N-dihydrogalactochitosan (GC), to mice with MMTV-PyMT tumors. To assess transcriptional alterations in B and T cells within the tumor microenvironment (TME), single-cell RNA sequencing (scRNAseq) was utilized. LAIT not only prolonged survival in tumor-bearing mice but also increased the presence of tumor-infiltrating B cells, activated CD8+ T cells, and naïve/memory CD4+ T cells. Both GC and combined PTT+GC therapies triggered activation markers in these cells. We observed an upregulation of interferon response genes and antigen presentation mechanisms in B cells, indicating a shift from a dormant to an active effector state. LAIT consistently stimulated co-stimulatory molecules and various antitumor cytokines, including type I/II IFNs, TNF, and IL1 in both CD8+ and CD4+ T cells. Concurrently, LAIT reduced immune-suppressing TGFβ signaling but slightly elevated immune checkpoints like *Pdcd1* (PD1) and *Ctla4* (CTLA4), providing a basis for combining LAIT with immune checkpoint blockade (ICB) for enhanced treatment efficacy. Gene expression patterns in both B and T cells were correlated with extended survival in breast cancer patients. Our study demonstrates that LAIT triggers a widespread proinflammatory response in lymphocytes, characterized by the activation of interferon signatures and antigen presentation in B cells, thereby remodeling the TME to bolster antitumor immunity. These insights support the potential of combining LAIT with immune checkpoint inhibitors for treating metastatic, resistant cancers, and emphasize the importance of lymphocyte activation in cancer therapy.

Keywords: Single-cell RNA sequencing (scRNAseq), localized ablative immunotherapy (LAIT), photothermal therapy (PTT), N-dihydrogalactochitosan (GC), tumor-infiltrating T/B cells, antitumor immune response

MULTI-OMIC ANALYSIS UNRAVELS THE PROGNOSTIC AND PREDICTIVE VALUE OF *LAG3* EXPRESSION IN UROTHELIAL CARCINOMA

Adanma Ayanambakkam, Anh Lam, Kieran Sweeney, Andrew Elliott, Chadi Nabhan, Rana R. Mckay, Abhishek Tripathi, Sumati Gupta, Xu Chao, Jad Chahoud, Debasish Sundi, Paul Skelton, Laura Graham, Lyudmyla Berim, Bodour Salhia, Sean Kern, Yousef Zakharia, Steven Edge, Abdul Rafeh Naqash

Background: Lymphocyte-activation gene 3 (*LAG3*) is an immune checkpoint protein expressed on immune cells that inhibits T-cell function. Despite its established prognostic significance in other malignancies, the role of *LAG3* as a prognostic or predictive biomarker in urothelial carcinoma (UC) remains inadequately studied.
Methods: DNA (592-gene or whole exome) and RNA (whole transcriptome) sequencing were performed for patient tumors submitted to Caris Life Sciences. PD-L1+ status (22c3, combined positive score≥10) was determined by IHC. TMB-High (TMB-H) was defined as ≥10 mutations/Mb. *LAG3* high (*LAG3*-H) and low (*LAG3*-L) groups were defined by the top and bottom quartiles of *LAG3* RNA transcripts per million, respectively. Tumor microenvironment (TME) cell fractions were estimated by RNA deconvolution using quanTIseq. Significance was tested using Mann-Whitney U and χ^2 tests as appropriate. Real-world overall survival (OS) was obtained from insurance claims data and calculated from treatment start to last contact, while time-on-treatment (ToT) was calculated from treatment start to end. Hazard ratio (HR) was calculated using the Cox proportional hazards model, and p-values were calculated using the log-rank test. Clinical and RNA-seq data from patients enrolled in the Oncology Research Information Exchange Network (ORIEN) were used to validate the analysis.
Results: Among 3343 UC cases, *LAG3*-H was associated with increased *TP53* (70.6% vs 49.4%, $q<10^{-4}$) and *RB1* mutations (31.0% vs 18.0%, $q<10^{-4}$), decreased *FGFR3* mutations (6.0% vs 18.1%, $q<10^{-4}$), and increased TMB-H (50.1% vs 36.7%, $q<10^{-4}$) and PD-L1+ status (71.0% vs 16.2% 22c3, $q<10^{-4}$). *LAG3*-H tumors had increased infiltration of CD8+ (1.5% vs 0.0%, $q<10^{-4}$) and NK (2.3% vs 1.6%, $q<10^{-4}$) immune cells, but also higher levels of inhibitory Tregs (3.3% vs 1.4%, $q<10^{-4}$). No statistically significant difference was found in OS of patients with LAG3-H, when comparing low vs high levels of FGL1 expression (HR=0.934, p=0.51). Among patients who received an immune checkpoint inhibitor (ICI; N=675), multivariate analysis using Cox proportional hazard regression revealed that *LAG3*-H had improved OS vs *LAG3*-L (HR=0.720, p=0.002) after accounting for potential confounders (sex, TMB, *TP53*, and *FGFR3*). *LAG3*-H also had significantly improved OS vs *LAG3*-L in PD-L1+ patients given ICI (N=291, HR=0.605, p=0.009). *LAG3* expression was also higher in patients with above median ToT on avelumab (1.4-fold, p=0.049) and pembrolizumab (1.2-fold, p=0.022). Improved OS for *LAG3*-H vs LAG3-L patients (HR=0.65, p=0.036) were validated using the ORIEN database.

Conclusions: Increased *LAG3* expression in UC correlates with a distinct mutational landscape, an inflamed TME characterized by augmented immune cell infiltration, prolonged ICI ToT, and significant improvements in OS. These findings corroborate the potential for dual LAG3 PD1 blockade in UC.

HONING IN ON SPATIAL TRANSCRIPTOMICS TO EVALUATE THE TUMOR MICROENVIRONMENT

Tae Gyu Oh, Ph.D.
Department of Oncology Sciences

Single-cell transcriptomics and spatial transcriptomics are cutting-edge technologies revolutionizing our understanding of cellular heterogeneity and spatial organization within tissues. In single-cell transcriptomics, individual cells are isolated and their RNA content is analyzed using high-throughput sequencing techniques. However, current droplet-based or microwell-based single cell profiling faces challenges such as technical variability, limited transcriptome coverage, and the potential for cell stress during sample preparation. Additionally, the presence of cell doublets and multiplets, coupled with the complexity of data analysis, adds layers of complexity to interpreting results.
Spatial transcriptomics goes beyond single-cell analysis by preserving the spatial context of gene expression within intact tissues. This technology allows researchers to map the transcriptomic landscape of tissues at single-cell resolution while retaining information about the spatial organization of cells within their native microenvironments. By capturing the spatial distribution of gene expression, spatial transcriptomics enables the exploration of tissue architecture, cell-cell interactions, and the spatial dynamics of cellular processes. In the Oh lab, we successfully established Xenium and Visium platforms (10X Genomics). In my discussion, I will discuss the advantages offered by spatial transcriptomics, highlighting its potential to unravel the spatial organization and high resolution within tissues. Additionally, I will address the drawbacks associated with this innovative technique, including technical challenges and data analysis complexities. Moreover, I will explore strategies aimed at overcoming these obstacles, facilitating more robust and insightful spatial transcriptomics analyses.

DETECTING NEOEPITOPE-SPECIFIC IMMUNE RESPONSE AND TCR REPERTOIRE DIVERSITY

Marmar Moussa*
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Recent advances in immune cell profiling in single cell resolution allow for antigen-specific T Cell Receptors identification and sequencing via highly specific barcoded multimers. Here we present a novel approach to identifying and profiling T Cell Receptor specificities in-silico and assess their diversity and phenotype in an integrated and interactive model. This method can be applied to viral as well as cancer specific epitopes using TCR sequencing data and single cell immune profiling assays. We implement metrics of sequence similarity, clonal expansion, gene usage, and define a novel metric for repertoire diversity based on graph-based network modularity optimization. Antigen and epitope-specific TCR sequencing data of putative cancer neoepitopes presented on MHC-I in mice is used to extract and engineer CDR3 sequence-based features and train a machine learning classifier for TCR specificity prediction. Additionally, our work integrates single cell RNA-Seq functional analysis for each tested epitope with its corresponding specificity and repertoire features.

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HEALTH PROMOTION RESEACH

Health Promotion Research Center Track — Samis Center Basement

2:00 – 3:05 PM

SESSION I: Tobacco Use / Cessation

Moderators: Darla Kendzor

2:05 – 2:25 PM

Measuring DNA Damage to Evaluate Electronic Cigarette Use as a Tobacco Harm

Vengatesh Ganapathy
Assistant Professor of Research
Department of Otolaryngology
University of Oklahoma Health Sciences

2:25 – 2:45 PM

Machine Learning Predictions of Smoking Trends Insights from the PATH Study

Hanxia Li
Graduate Student
College of Public Health
University of Oklahoma Health Sciences

2:45 – 3:05 PM

Empowering Our Community, Reclaiming Our Health: Developing a Community-engaged Smoking Cessation Pilot Intervention for Sexual and/or Gender Minoritized People in Oklahoma

Julia McQuoid
Assistant Professor
Department of Family and Preventative Medicine
University of Oklahoma Health Sciences

Taylor Ray
Freedom Oklahoma

3:20 – 4:25 PM

SESSION II: Cancer Disparities & Survivorship

Moderator:

3:25 – 3:40 PM

Disparities in Primary and Secondary Breast Cancers Among Women in Oklahoma

Amanda Janitz
Associate Professor
Department of Biostatistics & Epidemiology
University of Oklahoma Health Sciences

3:40 – 3:55 PM

Preliminary Feasibility and Acceptability of an Interdisciplinary, Single-session, Telehealth Class for Patients with Cancer-related Pain

Desiree Hilton Azizoddin
Assistant Professor
Department of Family and Preventative Medicine
University of Oklahoma Health Sciences

3:55 – 4:10 PM

Feasibility of Wearable Focal Vibration for Chemotherapy-induced Peripheral Neuropathy: Interim Results

Josiah Rippetoe
Graduate Student
Department of Rehabilitation Sciences
University of Oklahoma Health Sciences

4:10 – 4:25 PM

Impact of Tobacco Smoke Exposure on Cisplatin Efficacy in Head and Neck Cancer

Balaji Sadhasivam
Assistant Professor
Department of Occupational & Environmental Health
University of Oklahoma Health Sciences

MACHINE LEARNING PREDICTIONS OF SMOKING TRENDS: INSIGHTS FROM THE PATH STUDY

Hanxia Li, MSc[1], Sixia Chen, PhD[2]

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Background: Smoking remains a leading cause of preventable diseases, including cancer. Understanding and predicting smoking trends are crucial for effective public health interventions. The Population Assessment of Tobacco and Health (PATH) Study provides comprehensive data on tobacco use and its effects, presenting an opportunity to leverage machine learning (ML) for insightful analyses.

Objectives: This study aims to utilize machine learning techniques to analyze the PATH Study data, focusing on predicting smoking trends and identifying key factors influencing these trends.

Methods: We employed a range of machine learning algorithms, including decision trees, random forests, and neural networks, to analyze the PATH study dataset. Our approach involved data preprocessing, feature selection, and model training to predict smoking initiation, continuation, and cessation trends. We particularly focused on early-stage data to understand initial smoking behaviors.

Results: Preliminary results indicate that specific demographic, socioeconomic, and psychological factors play a significant role in smoking behaviors. Our ML models have shown promising accuracy in predicting smoking initiation and cessation trends. Notably, early indicators such as age of initiation and social influences were critical predictors in our models.

Discussion: The findings provide new insights into the dynamics of smoking behavior. The application of machine learning offers a novel perspective, highlighting patterns and predictors that traditional analysis might overlook. These results have significant implications for designing targeted public health strategies and interventions for smoking prevention and cessation.

Conclusion: Machine learning offers a powerful tool for analyzing complex behaviors such as smoking. Insights gained from the PATH study through ML techniques can guide public health policies and cancer prevention strategies, ultimately contributing to the broader goal of reducing smoking-related health burdens.

Keywords: Machine Learning, Smoking Trends, PATH Study, Public Health, Tobacco Control.

“EMPOWERING OUR COMMUNITY, RECLAIMING OUR HEALTH”: DEVELOPING A COMMUNITY-ENGAGED SMOKING CESSATION PILOT INTERVENTION FOR SEXUAL AND/OR GENDER MINORITIZED PEOPLE IN OKLAHOMA

Authors/Contributors (presenters indicated with asterisk):
Julia McQuoid,* PhD, University of Oklahoma Health Sciences Center
Taylor Raye,* Freedom Oklahoma
Mataia Blackwell, Freedom Oklahoma
David Bradley, University of Oklahoma Health Sciences Center
Darla Kendzor, University of Oklahoma Health Sciences Center
Erin Vogel, University of Oklahoma Health Sciences Center
Summer Frank-Pearce, University of Oklahoma Health Sciences Center
Arturo Durazo, University of California, Merced
Jaimee Heffner, Fred Hutch Cancer Center
Andy Tan, University of Pennsylvania
Sabrina Islam, University of California, San Francisco
Madelyne Wilson, University of Oklahoma Health Sciences Center
Margaret Le, University of Oklahoma Health Sciences Center

Tobacco-related inequities among sexual and/or gender minority (SGM) people persist, especially in places with high SGM stigma like Oklahoma. Tobacco is a leading cause of preventable cancer and death among SGM individuals, 35% of whom live in places with high structural stigma. These places tend to be more rural, expose SGM people to minority stressors (e.g., harassment), and have limited smoking cessation assistance, other health care, and SGM community participation opportunities. Existing SGM-tailored smoking cessation interventions overwhelmingly focus on within-person processes of behavior change rather than the adverse sociopolitical factors driving SGM smoking inequities. A promising but untested idea is that when SGM people in high-stigma environments participate in SGM-serving volunteer activities that empower their communities, they may also experience cognitive and behavioral changes that support smoking cessation (e.g., increased social support, lower internalized SGM stigma). Empowerment Theory (ET)-informed health behavior change approaches have worked for SGM HIV prevention and youth tobacco interventions. With our community partner, Freedom Oklahoma, and supported by a Stephenson Cancer Center Pilot Grant, we conducted a 12-week single arm pilot study (N=20) of an Empowerment Theory-based smoking cessation intervention for SGM people. Participants received remotely-delivered smoking cessation support through the SCC’s Tobacco Treatment Research Program and participated in online SGM-serving volunteer activities designed to benefit local SGM communities. This presentation will focus on the academic-community partnership through which we developed and pilot tested the intervention. Preliminary feasibility and acceptability outcomes from participant surveys and exit interviews will be presented. Intervention outcomes for our community partner will also be discussed.

PRELIMINARY FEASIBILITY AND ACCEPTABILITY OF AN INTERDISCIPLINARY, SINGLE-SESSION, TELEHEALTH CLASS FOR PATIENTS WITH CANCER-RELATED PAIN

Desiree R. Azizoddin[1,2], Sara DeForge[1], Ashton Baltazar[1], Kerry Bond[1], Raina Leckie[1], Jennifer Hardcopf Stagg[1], Blake T. Hilton[3], Jordan M. Neil[1, 2], Ryan Nipp[4], Beth Darnall[5], Robert R. Edwards[6]

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Background: Cognitive behavioral therapy for pain (pain-CBT) is the standard of care for pain management. However, few patients with cancer have access to this treatment. We developed a brief (90-minute), single-session, telehealth intervention that combines medical education (e.g., pain, opioids) with pain-CBT modified for patients with cancer. We sought to quantitatively and qualitatively evaluate the preliminary feasibility and acceptability of the class for patients with cancer-related pain.

Methods: Adults with chronic, cancer-related pain (≥4/10) who were receiving or recently completed treatment (<3 months) self-enrolled or were recruited from Stephenson Cancer Center (SCC) in Oklahoma between January and November 2023. We excluded patients who did not speak English or who were experiencing cognitive impairment. After consent, patients completed a baseline survey and attended the 90-minute class offered once monthly on Zoom™. Following attendance, the E-acceptability survey, with additional free-text feedback, and were invited to participate in a semi-structured qualitative interview. An initial benchmark for feasibility was set at ≥70% attendance.

Results: While recruitment is still ongoing, 116 participants have consented; 64 (55%) withdrew due to being too ill, no longer having pain, or being a fraudulent sign-up. Of the 52 (49%) remaining participants, 43 (82%) have attended the class; remaining participants are scheduled for future attendance. Participants were 69% female, 87% white, 53 (*SD* = 14.8) years of age, and diagnosed with various cancer types (gynecologic 27%, gastrointestinal 20%, head/neck 11%, etc.). Fourteen participants (27%) lived in rural Oklahoma. Thirty (68%) participants were taking opioids (short-acting=62%, long-acting=48%, both=35%). Average pain intensity (PROMIS Pain Intensity) was rated as 6.3/10 (*SD*=1.9). Attendees rated their overall satisfaction with the

class as 4.41/5. Participants enjoyed the class (4.20/5), reported learning about pain (4.24/5), and found the material useful (4.32/5) and helpful (4.07/5). Attendees found the class enjoyable and informational, with one stating, “this class [gave] me some tools to better manage my pain…and tools to be able to find help if I need it” (65-year-old, F).
Conclusions: To date, participants’ attendance in this single-session, interdisciplinary, telehealth cancer pain class was below our feasibility benchmark, with many requesting to attend future sessions or withdrawing due to being too ill or being lost to follow up. However, among those who have attended the class, they reported very high acceptability and satisfaction. Using qualitative interview feedback, we will tailor the intervention (e.g. more cancer-specific examples, provide a recording) to improve accessibility to this scalable, comprehensive cancer pain education class.

FEASIBILITY OF WEARABLE FOCAL VIBRATION FOR CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY: INTERIM RESULTS

Josiah Rippetoe, BS[1,2], Abby Cha, BS[1], Debra Richardson, MD[3], Kathleen Moore, MD, MS[3], Elizabeth Hile, PT, PhD[1,2]

[1]Cancer Rehabilitation, OU Health Stephenson Cancer Center, Oklahoma City, OK

[2]Department of Rehabilitation Sciences, College of Allied Health, OUHSC, Oklahoma City, OK

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Introduction: Up to 80% of individuals treated with neurotoxic chemotherapy experience chemotherapy-induced peripheral neuropathy (CIPN), and nearly 50% of those cancer survivors will have CIPN symptoms an average of 6 years later. CIPN doubles a survivor's age-predicted risk of falls and threatens their quality of life. Further, if symptoms restrict physical activity they could lead to sedentary behavior with negative health consequences. Although many approaches have been trialed, there is still no FDA-approved, universally effective treatment for CIPN. A promising non-invasive option is wearable focal vibration (FV) therapy. We aim to evaluate the feasibility and safety of using commercially-available FV to improve CIPN symptoms that have persisted at least 3 months after chemotherapy in patients with no active disease. Methods: In this early phase feasibility study with single-arm, repeated measures and optional double-baseline, participants apply FV to the leg of higher symptom burden for 2-4 daily sessions of 30-minutes each for 6 weeks. Outcomes are measured at Week 6 (immediate) and Week 12 (residual effect). We calculated adherence from device use logs as [completed sessions/ total assigned sessions (personalized)] and symptom response as 1-point of improvement on a 0-4 ordinal response scale using the validated Functional Assessment of Cancer Therapy/Gynecologic Oncology Group – Neurotoxicity (FACT/GOG-NTX). If the log was not returned, a participant's completed sessions were counted as 0. Results: At 73% of our target enrollment, we have enrolled 11 (84.6%) of 13 screened participants. One participant withdrew for personal reasons (9% attrition), and 9 (90%) of 10 retained have completed the 6-week intervention. Eight of them (88.9%) returned complete or partial device use logs. Participants are age 58 (±8) years, 67% female, 67% White Non-Hispanic or Latinos, 11% Asian, 11% American Indian (11% did not report). They are survivors of breast or gynecological (44.4%), GI (22.2%), and other (33.3%) cancers. Group adherence is 78% (656 completed /838 total sessions). Four participants (44.4%) reported Grade 1 adverse events while using FV, and two others (22.2%) reported Grade II events due to non-compliance. At Week 6, four participants (44.4%) improved in foot numbness/tingling, and three (75%) retained these gains at Week 12. Three participants (33%) reported no change in paresthesias, and two reported worsening. For CIPN pain, at Week 6 a total of six participants (66.7%) reported improvement; two of them (33.3%) retained the gains at Week 12. No participant reported an increase in pain

at Week 6 or 12. Conclusions: Six weeks of wearable FV is feasible for cancer survivors with persistent CIPN. We have had no Grade 3 or higher AEs. As many as 1 in 3 participants may experience residual reduction in their paresthesias or pain after FV is discontinued. Even if symptom management with this noninvasive wearable technology is transient, our results suggest that further study of FV is warranted, but with close attention to predictors of response.

Funding: Cancer Therapeutics / Cancer Prevention and Control Pilot Grant from the NCI Cancer Center Support Grant P30CA225520 to OUH Stephenson Cancer Center.

IMPACT OF TOBACCO SMOKE EXPOSURE ON CISPLATIN EFFICACY IN HEAD AND NECK CANCER

Balaji Sadhasivam[1,2,6], Jimmy Manyanga[1,3], Vengatesh Ganapathy[1], Mayilvanan Chinnaiyan[1], David Rubenstein[4], Pawan Acharya[5], Daniel Zhao[5], and Lurdes Queimado ✉[1,2,6]

Departments of [1]Otolaryngology Head and Neck Surgery, [2]Occupational and Environmental Health, [3]Cell Biology, and *[5]Biostatistics, [6]TSET Health Promotion Research Center, Stephenson Cancer Center, The University of Oklahoma Health Sciences Center, Oklahoma City OK-73104, USA.*
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Tobacco smoke (TS) is a preventable risk factor for cancer and other high-mortality diseases. The prevalence of TS among cancer survivors is 52% and the amount of tobacco use (active smoking) or level of exposure to secondhand tobacco smoke (SHS) is uneven. Our recently published patient data show that smoking cessation after head and neck squamous cell carcinoma (HNSCC) diagnosis and before therapy increases therapy efficacy, reduces cancer recurrence, and increases long-term survival. A sole study showed that SHS exposure is an independent predictor of HNSCC cancer recurrence. The mechanism behind TS exposure and HNSCC's poor treatment outcome is obscure. We investigated the impact of TS (both active and passive smoke) exposure on HNSCC cisplatin efficacy and characterized the underlying mechanisms. HNSCC cells (UM-SCC1, WSU-HN6, and WSU-HN30) were exposed to TS extracts for 48h at doses mimicking the nicotine levels observed in the user's plasma. Then, cancer cells were treated with cisplatin (0.1-100 μM) in the presence or absence of TS extracts. Compared to cisplatin alone treatment, cancer cells exposed to both cisplatin and TS extracts showed significantly lower cisplatin-induced cell death, higher cell viability, higher IC_{50}, and higher indefinite survival capacity. Exposure to both TS extracts, representative of active and passive smoke, significantly increases cisplatin resistance in HNSCC when compared with cisplatin alone treatment. However, exposure to TS extracts alone didn’t change cancer cell viability, cell death, or cell proliferation compared to unexposed control cancer cells. Furthermore, exposure to TS extracts significantly reduced the drug transporter (CTR1) and increased the multidrug-resistant proteins ATP7 and ABCG2, potentially reducing cisplatin intracellular availability. Future in vivo mechanistic studies mimicking active and passive tobacco exposure among cancer populations can provide substantial evidence to unearth elucidative clinical implications.

Funding: This work was partially supported by the National Cancer Institute of the National Institutes of Health (R33CA202898, R01CA242168, and P30CA225520), the Oklahoma Tobacco Settlement Endowment Trust, and the Oklahoma Center for Advancement of Science and Technology (HR16-007). Dr. Queimado holds a Presbyterian Health Foundation Endowed Chair in Otorhinolaryngology Position.

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POSTER PRESENTATIONS

POSTER SESSION

(Listed A-Z by Presenters First Name)

Samis Center Level 1

Poster Board #:	First Name:	Last Name:	Academic Appointment:	SCC Research Program Affiliation:	Title:
29	Abdulqader	Khormi	Graduate Student	Cancer Prevention and Control	LONGITUDINAL ASSOCIATIONS BETWEEN APPENDICULAR LEAN MASS AND STRENGTH WITH CUMULATIVE TAXANE-PLATINUM CHEMOTHERAPY FOR WOMEN'S CANCERS
28	Amanda	Janitz	Faculty	Cancer Prevention and Control	IMPLEMENTATION OF A FINANCIAL HARDSHIP SCREENING AMONG NATIVE AMERICAN PATIENTS WITH CANCER
3	Arpan	Dey Bhowmik	Postdoctoral Fellow	Cancer Biology	MICRORNA-195: A PROMISING CANDIDATE AGAINST OVARIAN CANCER THERAPEUTIC DEVELOPMENT
48	Barbara	Mensah Sankofi	Graduate Student	Cancer Therapeutics	FGF1 REGULATES GLYCOLYSIS THROUGH ETV4 IN OBESITY-ASSOCIATED BREAST CANCER
20	Blayne	Barker	Staff	Cancer Prevention and Control	THE RELATION BETWEEN DISCRIMINATION AND HEALTH BEHAVIORS IN RECENTLY INCARCERATED ADULTS EXPERIENCING HOMELESSNESS
47	Brooke	Meelheim	Clinical Fellow	Cancer Therapeutics	FGF7 IS A PROMISING TARGET IN THE PROCESS OF OVARIAN CANCER TUMOR ATTACHMENT TO PREVENT METASTASIS
4	Clay	Foster	Postdoctoral Fellow	Cancer Biology	*MYC*-DRIVEN REPLICATION TIMING AND TRANSCRIPTIONAL ABERRATIONS IN B- VS. T-LINEAGE ALL
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5	Mohan Shankar	Gopinatha Pillai	Postdoctoral Fellow	Cancer Biology	EVALUATING THE EFFECT OF NNT-AS1 MEDIATED REGULATION OF NNT IN PROGRESSION OF HIGH GRADE SEROUS OVARIAN CANCER
35	Nadine	Sikora	Graduate Student	Cancer Prevention and Control	MINORITY STRESS CORRELATES OF TOBACCO PRODUCT USE AMONG SEXUAL MINORITY ADULTS IN OKLAHOMA
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24	Olivia	Davis	Graduate Student	Cancer Prevention and Control	CHARACTERIZATION OF CUTANEOUS PTCL-NOS USING A NATIONAL CANCER DATABASE
16	Pallab	Shaw	Postdoctoral Fellow	Cancer Biology	ROLE OF CBS IN DIFFERENT CELL TYPES OF OVARIAN CANCER TUMOR MICROENVIRONMENT
10	Phoebe	Ohene-Marfo	Graduate Student	Cancer Biology	NON-NECROPTOTIC ROLES OF MLKL IN DIET-INDUCED OBESITY, LIVER PATHOLOGY, AND INSULIN SENSITIVITY
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6	Rami	Hassan	Graduate Student	Cancer Biology	DROSOPHILA MODEL OF HPV18-INDUCED PATHOGENESIS PROVIDES INSIGHT INTO ANTI-APOPTOTIC FUNCTION OF E6 ONCOGENE
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41	Richard	Bui	Graduate Student	Cancer Therapeutics	INHIBITION OF OVARIAN CANCER PROLIFERATION: TARGETING OXYSTEROL-BINDING PROTEINS AND INTRACELLULAR LIPID TRANSPORT

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7	Sabira Mohammed	Jazir	Postdoctoral Fellow	Cancer Biology	UNDERSTANDING THE LINK BETWEEN INFLAMMATION, NECROPTOSIS, AND AGING LIVER: IMPLICATIONS FOR NONALCOHOLIC FATTY LIVER DISEASE AND HEPATOCELLULAR CARCINOMA
42	Sampurna	Chakraborti	Graduate Student	Cancer Therapeutics	ADVANCING PRECISION ONCOLOGY: HARNESSING ANNEXIN A5-MEDIATED DRUG DELIVERY FOR ENHANCED CHEMOTHERAPY IN TRIPLE-NEGATIVE BREAST CANCER
33	Santny	Shanmugarama	Graduate Student	Cancer Prevention and Control	NOVEL, ENGINEERED FUSOGENIC LIPOSOME-BASED ANTI-OXIDANT DELIVERY SYSTEM IMPROVES THE BLOOD-BRAIN BARRIER INTEGRITY IN AGING
36	Sarah	Smith	Graduate Student	Cancer Prevention and Control	EPIDEMIOLOGY, CLINICAL CHARACTERISTICS, AND TREATMENT STRATEGIES OF POLYMORPHOUS ADENOCARCINOMA OF THE HEAD AND NECK
11	Spoorthy	Pathikonda Seelesh	Postdoctoral Fellow	Cancer Biology	EVALUATING THE FUNCTIONAL ROLE OF HISTONE ACETYLTRANSFERASES IN GLIOBLASTOMA RESISTANCE
54	Sreenidhi	Mohanvelu	Graduate Student		RD3 REGULATES DE NOVO FORMATION OF MUSCLE INVASIVE DISEASE FROM NON-MUSCLE INVASIVE BLADDER CANCER
43	Swati	Choudhary	Graduate Student	Cancer Therapeutics	UNVEILING PRECISION TARGETS: OSBP AND ORP4 IN OVARIAN CANCER THERAPY WITH OSW-1 ANALOG COMPOUNDS
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18	Tyler	Noble	Graduate Student	Cancer Biology	MECHANISMS DETERMINING WHERE DNA REPLICATION INITIATES IN THE HUMAN GENOME
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45	Zitha Redempta	Isingizwe	Postdoctoral Fellow	Cancer Therapeutics	COMBINATION EFFECTS OF SHETA2 AND CDK4/6 INHIBITORS IN OVARIAN CANCER

LONGITUDINAL ASSOCIATIONS BETWEEN APPENDICULAR LEAN MASS AND STRENGTH WITH CUMULATIVE TAXANE-PLATINUM CHEMOTHERAPY FOR WOMEN'S CANCERS

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Background: Breast and gynecological cancer survivors can lose significant muscle mass during chemotherapy; based on abdominal computed tomography (CT) at least 20% transition to sarcopenia which signals worse cancer outcomes and more severe chemotoxicities. In addition to this cachectic sarcopenia, chemotherapy-induced peripheral neuropathy (CIPN) can cause a muscle loss that is characterized by length-dependency: loss starts distally (toes or fingers) and progresses up the limb. In other populations, losing distal strength impacts balance and manual dexterity, abilities that are important to quality of life (QoL), and rehabilitative approaches differ when restoring muscle mass or neuromotor control. Purpose: In women receiving taxane-platinum therapies for breast and gynecological cancers, we aim to explore longitudinal associations between arm or leg appendicular lean mass (ALM) and the strength of the corresponding toe (hallux) or finger over successive chemotherapy cycles. Secondarily, we will explore longitudinal relationships to balance confidence and quality of life (QoL). Materials and Methods: We performed a secondary analysis of data from a feasibility study to prospectively monitor CIPN for up to five taxane-platinum chemotherapy cycles for women's cancers. We used bioimpedance spectroscopy to quantify bilateral arm and leg ALM, dynamometry for grip and pinch strength, and our patented QuHalEx device for hallux flexion and extension strength. We administered the Activities-Specific Balance Confidence (ABC) scale to quantify patient-reported balance, and Functional Assessment of Cancer Therapy-Taxane-Total Outcome Index for QoL. We employed stepwise linear mixed models in R (alpha =.05) using limb-specific ALM as predictive variables. Results: Participants were 32 women aged 64.5 ± 11.9 years (6% Black, 3% Asian, 3% Two or more races; 6% Hispanic/ Latina) with gynecological (87.5%) or breast cancers. Arm or leg lean mass associated with strength for finger pinch or hallux extension, respectively. A 1-lb decline in left arm ALM predicted a 1.03 lb decline in left pinch strength (p=0.02). A 1-lb decline in leg ALM predicted 0.42 (right, p=0.029) and 0.43 (left, p=0.009) lb declines in hallux extension strength. We found no associations between ALM and hand grip or hallux flexion strength, although right hallux flexion decreased by 0.57 lb with each chemotherapy cycle

($p<0.021$). The only strength change that was significantly associated with balance confidence was pinch ($p=.037$ right, $p=.028$ left), and balance confidence was the only variable to predict QoL ($p<0.0001$). QoL decreased by 3.65 points per cycle ($p=0.004$). Conclusions: In this small cohort with women's cancers, exploratory analyses suggest that losing lean mass in a limb during chemotherapy contributes to losing strength in finger pinch and hallux extension, but not in hallux flexion, so different strategies may be required for neurorehabilitation. The length-dependent nature of neurotoxicity may explain why losing pinch strength (as a proxy for more severe CIPN) but not hallux strength related to declines in balance confidence, which then predicted QoL decline in this cohort. We plan a future study with full power to quantify the contributions of muscle loss to losses of distal strength during neurotoxic chemotherapy.

This project was funded by the Presbyterian Health Foundation (PHF) University of Oklahoma Health Sciences Center (OUHSC) College of Allied Health New Investigator Seed Grant to Elizabeth Hile, the Oklahoma Tobacco Settlement Endowment Trust (TSET) and the National Cancer Institute Cancer Center Support Grant P30CA225520 awarded to the University of Oklahoma Stephenson Cancer Center.

IMPLEMENTATION OF A FINANCIAL HARDSHIP SCREENING AMONG NATIVE AMERICAN PATIENTS WITH CANCER

Janitz AE, Anderson-Buettner AS, Madison SD, Doescher MP, Rhoades DA

Introduction: Financial hardship and financial hardship screening are emerging concerns in oncology. Native American patients may be at increased risk of financial hardship due to factors including poverty, medical comorbidities, and lack of private health insurance coverage. Financial hardship for Native American patients with cancer has only rarely been studied, and implementation of screening for financial hardship for these patients has never been reported.
Methods: Guided by input from a stakeholder advisory board consisting of patient, provider, and staff members at a single cancer center in Oklahoma, we implemented a financial hardship screening tool, the COmprehensive Score for financial Toxicity (COST) – Functional Assessment of Chronic Illness Therapy (FACIT) among 42 Native American patients with cancer. We conducted key informant interviews with ten of these patients and four clinical staff involved in the implementation process. Patient interviews included questions about current financial hardship, experiences in discussing financial hardship with the cancer care and primary care team, and acceptability of the COST-FACIT tool. Clinician interviews focused on their experience with the project, including implementation of the COST-FACIT tool, barriers to implementation, and sustainability. Recorded interviews were transcribed and thematically analyzed using MAXQDA® software. COST-FACIT tool data were analyzed using SAS v. 9.4
Results: Three-quarters (76%, n=32) of participants who completed the COST-FACIT tool reported moderate or severe financial hardship (Score <25 out of max 44, with lower scores indicating more hardship). A higher percentage of patients experiencing financial hardship were younger, covered by Medicaid, unemployed, not married/cohabiting, had lower income, and lower education compared to those with no/mild hardship (Scores ≥25). Among patients and clinicians, we identified themes of 1) financial hardship screening perception and intervention experiences, 2) screening efficacy and opportunities for improvement, and 3) systematic and patient related themes of Native American health systems and culture.
Conclusions: Financial hardship was reported by the majority of Native American patients with cancer included in our study. Patients expressed a positive experience with the screening tool, including identification of financial challenges though timing of the tool in regards to their cancer diagnosis varied across patients. Clinicians experienced challenges in implementation of the COST-FACIT tool related to logistics, the COVID-19 pandemic, and concerns for sustainability. However, clinicians reported a positive experience with the tool and interactions with patients and referrals that resulted from the screening.

MICRORNA-195: A PROMISING CANDIDATE AGAINST OVARIAN CANCER THERAPEUTIC DEVELOPMENT

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Background: Ovarian cancer confers highest mortality rates among the gynaecological malignancies. Diagnosis at advanced stages, drug resistance and reoccurrence are the main reasons of high mortality. Studies suggest 'Cancer Stem Cells' (CSCs) has the capacity to regrow the cancer after treatment and making the cancer more aggressive by causing drug resistance. MiR-15/107 family member miR-195 controls various pathways that are instrumental in maintaining CSCs. Our previous study revealed decreased expression of miR-195 in ovarian cancer patient samples, ovarian cancer cell lines and ectopic expression inhibits clonal growth and invasion. The miR-195 re-expressing group had significantly lower tumor volumes and greater tumor doubling time over control.

Hypothesis: In this background, we hypothesized that miR-195 may regulate ovarian cancer progression by targeting stem cell population.

Methods: The functional enrichment of the ovarian cancer stem cell population was done by growing them as an anchorage-independent spheroid, as it mimics the ovarian cancer metastatic process and has been reported to have enhanced stem cell-like properties. To confirm the enrichment of cancer stem cell population, immunoblotting of cancer stem cell markers were performed. To correlate the expression of miR-195 in a cancer stem cell-enriched population, RT-QPCR was carried out in OC90 and OVCAR cells. To further confirm the role of miR-195 in the ovarian cancer stem cell population, OV90 cells were transiently transfected with either non-target miR control (miR-CTL), miR-195, or anti miR-195 and relative expression of stem cell markers was evaluated.

Results: Ovarian cancer spheroid were enriched in stem cell population which was confirmed by the enhanced expression of cancer stem cell markers NANOG, OCT4, cMYC, SOX2, ALDH1A, KLF4. Interestingly in this spheroid, miR-195 expression was significantly decreased as compared to cells grown as monolayers. To confirm the regulation of stemness is mediated through miR-195, we measured the NANOG expression in ovarian cancer cells transfected with either miR control (miR-CTL), miR-195, or anti miR-195, and observed decreased NANOG expression with miR-195 over-expression, while increased NANOG levels with the anti-miR-195 transfection compared to the miR CTL suggesting, expression of miR-195 is associated with ovarian cancer stemness. In order to gain a thorough understanding of miR-195-mediated signaling in ovarian cancer, mass spectrometry was carried out. Several canonical pathways were found to be inhibited, including EIF2 signaling, ELF4 signaling, and

p70S6K signaling in miR-195 overexpressed OV90 cells. Importantly, the over-expression of miR-195 effectively inhibits pathways associated with malignant solid tumors, as well as colony formation, which serves as a measure of stemness and *in vivo* tumor growth rate. Conversely, we observed significantly activated pathways related to CDKN2A, FOXO3, and TRIB3, which are associated with cell cycle regulation and increased apoptosis. Notably, our upstream regulator analysis revealed a significant increase in TP53-associated signaling, whereas MYC-mediated signaling was profoundly inhibited.

Conclusions: Conventional therapies, including chemotherapy and radiotherapy, target the larger population of rapidly proliferating cancer cells. Although a large proportion of the tumor mass may be eradicated but therapy-resistant CSCs remain and over time they can grow into tumors with more aggressive phenotype than the primary malignancy. In this context, miR-195 has shown potential to combat this scenario and cumulatively, our results support that miR-195 is a potent therapeutic target for ovarian cancer.

FGF1 REGULATES GLYCOLYSIS THROUGH ETV4 IN OBESITY-ASSOCIATED BREAST CANCER

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Obesity is associated with resistance to breast cancer endocrine therapies and excess patient mortality, particularly for estrogen receptor-positive (ER+) tumors that represent 70% of all cases. Adult weight gain in women with obesity, characterized by adipose tissue expansion, is an independent prognostic factor for breast cancer. In a preclinical model, we found that weight gain promoted ER+ tumor growth after endocrine therapy through adipose-derived FGF1. To determine the underlying mechanisms, we used tamoxifen-resistant MCF7 cells (TAMR) treated with FGF1 *in vitro*, combined with gene expression profiling and metabolic analysis. ETS variant 4 (ETV4), which regulates ER activity and breast cancer cell glycolysis, was the top gene induced by FGF1 in multiple ER+ lines, including TAMR cells. ETV4 was also upregulated in human PDX tumors grown in obese versus lean mice. In invasive human breast cancer specimens, high versus low ETV4 expression predicted a shorter recurrence-free survival for patients with ER+ tumors. In TAMR cells, FGF1 increased glycolysis but not mitochondrial respiration in the presence of glucose and glutamine, accompanied by elevated glycolytic gene expression and cell proliferation.
We hypothesized that ETV4 induction by FGF1 mediates altered ER activity and glycolytic metabolic reprogramming in obesity-associated breast cancer cells. ETV4-knockout TAMR cells failed to induce glycolytic genes and activity after FGF1 treatment compared to wild-type cells, and this associated with lower cell proliferation. In addition, loss of ETV4 led to a decrease in glucose substrate oxidation in TAMR cells. Taken together, our data suggest that FGF1 promotes breast cancer endocrine therapy resistance in the context of obesity through ETV4 induction and metabolic reprogramming. The ability to preferentially use a variety of metabolic substrates may provide an advantage to cancer cells growing in a nutrient-rich environment, and ETV4 may serve as a biomarker for patients at high risk for progression.

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MYC-DRIVEN REPLICATION TIMING AND TRANSCRIPTIONAL ABERRATIONS IN B- VS. T-LINEAGE ALL

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The involvement of the proto-oncogene *MYC* in human cancer is well known, but the mechanism(s) behind its neoplastic potential remain unclear. *MYC* is known to play a key part in the development of acute lymphoblastic leukemia (ALL), a molecularly diverse and lethal form of pediatric cancer. ALL arises in immature B and T lymphocytes (B- and T-ALL, respectively). To investigate the roles of MYC in B- and T-ALL, we developed a transgenic zebrafish model encoding human *MYC* (*hMYC*) to drive the development of both lineages of the disease. MYC is a master transcription factor often overexpressed in ALL and in many other cancers. It is known to also affect non-transcriptional processes, such as DNA replication timing, though how this affects leukemogenesis is currently unknown. We hypothesize that MYC alters transcription and replication timing in *hMYC*-driven B-/T-ALL in a systematic manner, revealing common and cell type-specific characteristics directly related to leukemogenesis. We speculate that these will include novel therapeutic targets and biomarkers for the treatment and detection of ALL. Using Next Generation Sequencing (NGS) and the *hMYC* model, we will investigate the effect(s) of MYC overexpression as a function of malignancy. Preliminary comparisons of transcription and replication timing profiles via NGS data revealed a global correlation between the processes, independent of cell type. Smaller regions of derangement unique to each lineage and related to MYC overexpression were also observed. To evaluate the significance of these regions, we mapped the MYC regulome using CUT&RUN sequencing to generate a list of loci directly bound by MYC. The overlap between these results will reveal genomic regions of dysregulated transcription and replication that are directly affected by hMYC overexpression and DNA binding as a function of malignancy. We speculate that genes within the affected loci play key mechanistic roles in leukemogenesis for both cell types in our *hMYC*-driven ALL model, and we now seek to reconcile our findings with human ALL patient data to identify the most clinically relevant candidate genes. These genes will be used for further functional studies to identify novel therapeutic targets and biomarkers for the treatment and detection of pediatric ALL.

GENOME-WIDE SCREENS FOR NOVEL DNA REPLICATION FACTORS

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During each round of cell division, cells must faithfully duplicate their DNA. DNA replication occurs at tens-of-thousands of individual sites or "origins", along the DNA strands through a highly coordinated process. While genetic screens in yeast have been invaluable for the identification of proteins involved in DNA replication origin firing and DNA fork elongation, mammalian cells have a larger genome, a more complex and diverse chromatin landscape, and are governed by additional regulatory mechanisms. To identify novel regulators of DNA replication initiation, we performed genome-wide CRISPR/Cas9 sgRNA knockout screens in human HCT116 cells in which all alleles of two crucial replication initiation factors, CDC45 or MTBP were fused to an auxin-induced degron. Both cell lines display weakened DNA replication and impaired proliferative capacity following exposure to Auxin. We used the BrunelloV2 sgRNA library, targeting 19,114 human genes, to identify genes whose loss either suppressed or enhanced the defective proliferation phenotype in these cells, both with and without Auxin treatment. Results from our screens have led to the identification of novel candidate genes, suggesting a broader network of genes may function the control of DNA replication in human cells.

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RELATIONS BETWEEN CHRONIC CONDITIONS (MENTAL AND PHYSICAL) AND FEELING TIRED ARE MODERATED BY DAILY HEALTH BEHAVIORS

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Background: Many US adults report a chronic health condition and reports of feeling tired are common among those with chronic conditions. Feelings of tiredness can prevent individuals from completing important daily tasks and can increase risks for negative health outcomes. Few studies have examined if daily health behaviors moderate relations between chronic health conditions and daily feelings of tiredness.

Methods: Data are from a large nationwide study that aimed to examine best practices for smartphone-based daily surveys. Participants completed a baseline survey and 2-4 daily surveys for 28 days. Generalized linear mixed models examined the effects of chronic health conditions (mental illness [e.g., anxiety/depression] or chronic physical condition [e.g., arthritis, cancer]) on daily reports of tiredness. Participants answered daily questions about feeling tired on a 5-point Likert-type scale for 14 days, and a slider-type scale for 14 days. Moderation analyses examined whether daily health behaviors (i.e., sleep hours, alcohol use, minutes of total physical activity) moderated the relationship between chronic health conditions and feelings of tiredness. Covariates (i.e., age, income, sex at birth, race) were included in all models.

Results: Participants (N = 460) were 48.4 years old (SD = 12.2), mostly White (71.5%), and female (77.2%). Presence of a chronic condition (mental or physical health) was consistently associated with higher levels of daily tiredness (all p's<.05). Follow-up analyses indicated that daily sleep hours moderated the impact of mental illness on daily tiredness (Likert) such that those with a mental illness who slept more reported feeling disproportionately more tired than those without a mental illness. However, increased sleep appeared to reduce the tiredness (slider) gap between those with and without chronic physical conditions. Increased alcohol use and higher levels of exercise appeared to attenuate the relationship between presence of a mental illness and tiredness. All other models were non-significant.

Conclusion: Chronic mental and physical health conditions are related to increased daily reports of tiredness, and daily healthy behaviors may attenuate tiredness. Specifically, increased sleep and increased physical activity may reduce tiredness, and should be considered for inclusion in treatment plans. Future analyses should further examine measurement scale effects on study outcomes.

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ADVANCED NANOMATERIALS-BASED SORBENTS FOR MEASUREMENT OF SHORT-DURATION, CARCINOGENIC VOC EXPOSURES

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Occupational exposure to volatile organic compounds (VOCs) is a significant concern due to their potential carcinogenic and mutagenic effects on human health. Monitoring these exposures is crucial as both low concentrations and short-term exposure have been linked to cancer development. Traditional methods, utilizing active and passive samplers, are commonly used, but the applicability of passive samplers in scenarios with short durations and low concentrations is challenging. This study explores the efficacy of buckypapers (BP) made from single-wall carbon nanotubes (SWNT) for evaluating short-term and low-concentration VOC exposures. Three buckypapers, fabricated from both functionalized (FX) and non-functionalized SWNTs, were exposed to four representative VOCs (Toluene, Trichloroethylene, n-Hexane, and 2-propanol) to assess their adsorption capacities. The adsorption capacities of 50 mg buckypapers (FX00, FX50, and FX90) at 300 ppm equilibrium concentration for each VOC are as follows: Toluene (82.9±8.1 mg/g, 90.4±4.1 mg/g, 51.4±2.4 mg/g), Trichloroethylene (97.0±14.5 mg/g, 95.9±3.4 mg/g, 39.1±1.8 mg/g), n-Hexane (32.8±6.2 mg/g, 33.5±1.9 mg/g, 21.5±2.9 mg/g), and 2-Propanol (22.6±5.43 mg/g, 36.9±0.75 mg/g, 21.53±0.12 mg/g). Statistical analysis using one-way ANOVA at α=0.05 revealed significant mean differences in the adsorption capacity across BP types for specific VOCs. F-50 buckypaper exhibited the highest overall adsorption capacity. In conclusion, this study highlights the considerable adsorption capacity of SWNT buckypapers and the potential of blending different SWNT types to tailored sorbents for collecting difficult-to-sample VOCs such as benzene, formaldehyde, acrolein and tobacco specific nitrosamines, contributing to the comprehensive evaluation of human exposures to VOCs in occupational settings and intermittent environmental exposures.

Keywords: VOC Exposure, Buckypapers, Adsorption capacity, Single-wall Carbon Nanotubes, Carcinogen

ASSAY VALIDATION OF HIGH-QUALITY CANCER BIOMARKERS FOR CLINICAL STUDIES

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The high mortality rate of ovarian cancer is due to late-stage detection and development of resistance despite high initial response rates to chemotherapy in about 60-70% of patients. Recent advances in ovarian cancer patient care involve maintenance therapy, administered after standard care, and standard-of-care surgery to delay recurrence. The maintenance therapy drugs bevacizumab, olaparib, niraparib, or rucaparib have proven effective in prolonging disease-free survival for ovarian cancer patients after response to platinum-based treatment, with the largest impact in front-line maintenance. However, these maintenance therapies are limited by the development of unacceptable toxicities and recurrence in most patients. Thus, monitoring ovarian cancer patients for recurrence is essential for deciding when to stop maintenance therapy, image patients, and administer additional chemotherapy or second-line drugs. Currently, the only blood-based biomarker assay used to monitor patients for recurrence is a cancer antigen 125 (CA-125) measurement. However, effective use of this assay is limited by moderate sensitivity and specificity. We aim to develop an assay to complement or improve CA-125 to facilitate ovarian cancer patient management decisions by multiplex multi-p53 mutant target proteins. This presentation will discuss our pyrenyl-nanocarbon-based electrochemical immunosensor measuring cancer protein concentrations in clinical serum solutions. Using serum samples, our sensor array facilitates the detection of p53 protein in ovarian cancer patients, providing a minimally invasive detection method. The sensor's remarkable ultra-low detection capability of picomolar concentrations of the p53 markers ensures reliable and consistent detection.

HEALTH-RELATED FACTORS ASSOCIATED WITH CANNABIS USE

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Background: Prior research has indicated mixed associations between cannabis use, physical health, and mental health. The primary aim of this study examined associations between cannabis use and health related outcomes in a large nationwide sample.

Methods: Participants enrolled in a nationwide trial that aimed to identify best practices for achieving high rates of smartphone-based survey completion. Participants downloaded the study smartphone application and used it to complete a baseline survey, 2-4 daily surveys for 28 days, and a follow-up survey. During the follow-up survey, participants answered questions about their past month cannabis use, days of poor physical health, and several mental health measures including the Short Scale Anxiety Sensitivity Index (SSASI), the Overall Depression Severity and Impairment Scale (ODSIS), and the Overall Anxiety Severity and Impairment Scale (OASIS). Linear regression analyses separately examined relationships between cannabis use status and days of medical and recreational cannabis use and days of poor physical health and SSASI, ODSIS, and ODSIS scores.

Results: Participants (n=454) were predominately White (71.4%), 48.1 years of age (SD=12.3), and female (77.1%). Overall, 98 participants reported using cannabis at least once in the past 28 days at follow-up, with 13.9 (SD=12.4) medical and 9.7 (SD=11.3) recreational cannabis use days on average (out of a possible 28 days). After accounting for covariates (i.e., race, age, education, sex, and chronic illness/mental health diagnosis), models showed that any past month cannabis use was associated with more days of poor physical health (p=0.027), more days of medical cannabis use was associated with more days of poor physical health (p=0.002), and more days of recreational marijuana use was associated with higher ODSIS scores (p=0.026). Further, more days of medical cannabis use, and more days of recreational cannabis use were associated with higher OASIS scores (p's=0.006 and 0.008, respectively).

Conclusion: Cannabis use may be associated with less physically healthy days and greater mental health symptoms. Future research should use a multi-method approach to investigate daily differences in physical health and mental health symptoms before and after cannabis use.

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SYNERGISTIC EFFECTS OF LASER IMMUNOTHERAPY AND IMMUNE CHECKPOINT INHIBITORS IN A MURINE MODEL FOR METASTATIC CANCER

Jacob Adams

Cancer is a leading cause of death around the world. While many types of cancer can be treated and even cured if detected early enough, later-stage, metastatic cancers often prove to be difficult to treat. Traditional modalities, like surgery and radiation, prove to be less effective against metastatic cancers. Alternatives to these treatments include various immune therapies that target the tumor, such as immune checkpoint inhibitors (ICI) which block certain molecules or receptors like programmed cell death 1 (PD1) and programed cell death ligand 1 (PD-L1). These therapies aim to break the checkpoints to help the immune system fight the cancer. Several other targets for ICI, like lymphocyte activation gene 3 (LAG3) and interleukin 6 (IL6), when blocked, lead to enhanced antitumor immune responses. Additionally, laser photothermal therapy (PTT) has shown success in reducing tumor burden. Furthermore, a novel therapy, laser immunotherapy (LIT), a combination of PTT with an immunostimulant, glycated chitosan (GC), induces a systemic, tumor-specific immune response in metastatic tumors. We propose that combining LIT with ICIs will provide stronger immune responses and increase the survival of mice with aggressive metastatic cancers. In this study, we investigated the effects of combining LIT with anti-LAG3 and anti-IL-6, using a metastatic mouse melanoma model. In our preliminary experimental results, we found that LIT synergizes with ICI by increasing tumor-infiltrating T cells to enhance the function of ICI.

Keywords: Metastatic tumors, immune checkpoint inhibitors, laser photothermal therapy, glycated chitosan

2020 POPULATION UPDATES FOR CANCER SURVEILLANCE: AN OKLAHOMA EXPERIENCE

JE Campbell, AB Sambo, M Doescher, AE Janitz

This study investigates the impact of the 2020 census population estimates' change on age-adjusted cancer incidence and mortality rates, particularly focusing on the American Indian and Alaska Native (AIAN) population in Oklahoma. The shift from bridged-race population estimates to recognizing a mixed-race population posed challenges in accurately assessing morbidity and mortality rates. The discontinuation of bridged estimates significantly affects the AIAN population, which already exhibits high age-adjusted mortality rates.

Utilizing Oklahoma's public health dataset assessed through OK2SHARE, the study compares rates calculated using bridged-race estimates and the new six-race categories introduced in the 2020 census. The analysis explores sociodemographic variations and trends over time, emphasizing the importance of understanding changes not attributed to healthcare practices but rather to alterations in the coding system.

Findings indicate minimal sociodemographic differences between bridged estimates and the 2020 race categories, except for age disparities. While overall cancer rate changes were not statistically significant for most racial groups, a striking decrease in AIAN population rate ratios was observed. Specific cancers showed varying patterns, with some experiencing statistically significant decreases in rate ratios.

This research sheds light on the complexities of adjusting cancer rates following demographic changes, particularly within the AIAN population in Oklahoma. The study's strengths lie in publicly available data and a focus on a region with a substantial AIAN population, providing insights into the challenges and implications of transitioning to new population estimates. However, limitations exist in the absence of a single comprehensive metric to fully capture AIAN disparities, highlighting the need for ongoing data refinement and awareness of potential misclassification issues.

TARGETING OF CYP2E1 BY MIRNAS IN ALCOHOL-INDUCED INTESTINE INJURY

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Although binge alcohol-induced gut leakage has been studied extensively in the context of reactive oxygen species (ROS)-mediated signaling, it was recently revealed that post-transcriptional regulation plays an essential role as well. Ethanol (EtOH)-inducible cytochrome P450-2E1 (CYP2E1), a key enzyme in EtOH metabolism, promotes alcohol-induced hepatic steatosis and inflammatory liver disease, at least in part by mediating changes in intestinal permeability. For instance, gut leakage and elevated intestinal permeability to endotoxins have been shown to be regulated by enhancing CYP2E1 mRNA and CYP2E1 protein levels. Although it is understood that EtOH promotes CYP2E1 induction and activation, the mechanisms that regulate CYP2E1 expression in the context of intestinal damage remain poorly defined. Specific miRNAs, including miR-132, miR-212, miR-378, and miR-552, have been shown to repress the expression of CYP2E1, suggesting that these miRNAs contribute to EtOH-induced intestinal injury. Here, we have shown that CYP2E1 expression is regulated post-transcriptionally through miRNA-mediated degradation, as follows: 1) the RNA-binding protein AU-binding Factor 1

(AUF1) binds mature miRNAs, including CYP2E1-targeting miRNAs, and this binding modulates the degradation of corresponding target mRNAs upon EtOH treatment; 2) the Serine/Threonine kinase MST1 mediates oxidative stress-induced phosphorylation of AUF1. Those findings suggest that ROS-mediated signaling modulates AUF1/miRNA interaction through MST1-mediated phosphorylation. Thus, our study demonstrates the critical functions of AUF1 phosphorylation by MST1 in the decay of miRNAs targeting CYP2E1, the stabilization of CYP2E1 mRNA in the presence of EtOH, and the relationship of this pathway to subsequent intestinal injury.

TRANSGENE ELECTROPORATION INTO ADULT ZEBRAFISH TO INDUCE ACUTE LYMPHOBLASTIC LEUKEMIA

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Zebrafish *(Danio rerio)* are gaining popularity as a more cost-effective cancer model due to their small size, high fecundity, ease of imaging, and variety of genetic manipulation techniques. One such technique, Transgene Electroporation into Adult Zebrafish (TEAZ) was developed in 2018 as a means to induce a highly aggressive model of melanoma. TEAZ allowed the malignancy to be somatically induced, granting greater spatio-temporal control of disease onset and improved visualization of metastasis. Additionally, onset of the somatically-induced melanomas was observed within ~7 weeks post-injection, twice as fast as previous germ-line mutant models. We have further adapted the TEAZ system to explore Acute Lymphoblastic Leukemia (ALL). ALL is a heterogeneous, hematologic disease caused by the proliferation of immature lymphoid cells in the bone marrow, peripheral blood, and other organs. It is the most common pediatric malignancy and second-most lethal pediatric disease in the United States. Several Zebrafish ALL models exist that present and respond to treatment in a manner similar to the corresponding human ALL. However, the majority utilize functionally relevant germ-line mutations to drive oncogenesis, lacking the increased spatio-temporal control and visualization advantages of TEAZ. By using TEAZ-induced ALL in zebrafish, we will be able to study ALL formation and progression from onset to metastasis in a time and site-specific manner.

MODULATION OF HR-HPV VIRAL PROTEIN E7 BY SHETA2 IN CERVICAL CANCER

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Introduction: The purpose of this study is to determine the effect of the chemotherapeutic sulfur heteroarotinoid A2 (SHetA2) on high-risk human papillomavirus (HR-HPV) proteins and the modulation of cell survival and proliferation in cervical cancer. Cervical cancer is caused by persistent HR-HPV infection. HR-HPV tumorigenesis is driven by its early 6 and 7 (E6, E7) oncoproteins, which increase cell proliferation and survival. Cellular pathways regulated by E6 and E7 are counter-regulated by the investigational new drug SHetA2, which is currently in phase 1 clinical trial for advanced and recurrent cancers. SHetA2 disrupts complexes of 70-kDa heat shock protein (HSP70) family members, hsc70, GRP78 and mortalin, with their client proteins. We hypothesized that SHetA2 reduces E6 and E7 levels and their binding to HSP70 chaperones in association with reduction of cervical cancer cell and tumor growth.

Methods: SHetA2 effects on specific genes and proteins in HR-HPV-positive cervical cancer cell lines and xenograft tumors were assessed by western blot, quantitative polymerase chain reaction, immunofluorescence ligation assays and coimmunoprecipitation assays.

Results: SHetA2 significantly reduced E6 and E7 mRNA, and protein levels of E7 and the E7-regulated p16, but not E6 in cervical cancer cells and xenograft tumors. MG312-inhibition of proteasome function attenuated the E7 reduction. HSP70/hsc70 proteins bound E7 and SHetA2 disrupted these complexes.

Conclusions/Implications: SHetA2 reduces E7 proteins in cervical cancer cells through a mechanism that involves proteasomal degradation in association with disruption of HSP70/E7 complexes, p16 reduction and decreased cell and tumor growth. This is the first demonstration of HSP70/E7 complexes. SHetA2-induced release of E7 from HSP70s could be causing increased susceptibility of E7 to proteasomal degradation. This data support development of SHetA2 and HSP70 inhibitors for cervical cancer.

A TRUNCATED FORM OF MULTIDRUG RESISTANCE PROTEIN 1 (MRP1) IN PLASMA SEVS IS A POTENTIAL INDICATOR OF GASTROINTESTINAL MALIGNANCIES

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MRP1/ABCC1 is an ATP-dependent transmembrane efflux pump that confers drug resistance. MRP1 is overexpressed in GI malignancies such as pancreatic ductal adenocarcinoma (PDAC) and colon cancer. Several proteomics studies have revealed the presence of MRP1 in small extracellular vesicles (sEVs) released from cancer cells. The cancer-derived sEVs are known to be released into the circulation, making them attractive candidates for non-invasive biomarker development. However, whether the MRP1 level in plasma sEVs is indicative of human cancer has not been evaluated. This study examined the MRP1 expression in plasma sEVs derived from patients with PDAC, colon and breast cancer, with age- and gender-matched healthy subjects. The human plasma samples were obtained from the NCI-sponsored Cooperative Human Tissue Network, Stephenson Cancer Center and Oklahoma Blood Institute. Human pancreatic cancer cell lines PANC-1, MIA PaCa-2 and BxPC-3, and pancreatic ductal cell line hTERT-HPNE were tested for MRP1 expression. Cellular and plasma sEVs were isolated using a double-filtration followed by polymer precipitation method. Western blot was performed to assess the expression level of MRP1 and proteomics was applied to confirm the detection of a truncated form of MRP1 in plasma sEVs. MRP1 was detected in the sEVs derived from all three pancreatic cancer cell lines but absent in the sEVs from HPNE. Overexpression of a truncated MRP1 protein was detected in plasma sEVs derived from patients with early and late stage PDAC, compared with healthy subjects (n=22). Similar findings were evident in patients with colon cancer (n=18), while the results remained inconclusive for patients with breast cancer (n=10). The truncated form of MRP1 was only detected using antibodies against the epitopes in the C-terminus and QCRL-1 region of MRP1 protein. Furthermore, proteomic analysis detected the peptides in the C-terminus region of MRP1. In summary, we have detected a truncated form of MRP1 protein in the plasma sEVs and its expression level is significantly elevated in patients with PDAC and colon cancer.

MECHANISMS OF DRUGS IN OVARIAN CANCER AND PREVENTION OF INVASION AND METASTASIS

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A critical hallmark of ovarian cancer is the early and quick spread of peritoneal metastases with about a five-year estimated survival for most cases. The formation of ovarian cancer is proposed to arise from precursor lesions in epithelial cells in the Fallopian tubes. Lesions will acquire more mutations that eventually lead to carcinogenesis. This development leads to most ovarian cancer cases being diagnosed at an advanced stage. Therapies are limited by toxicities and have no overall impact on survival, additionally, even with new therapies 80% of patients recur in three years with resistant and more aggressive forms of ovarian cancer . SHetA2 is a novel small molecule, in Phase 1 clinical trials, that binds to Grp78, Hsc70, and mortalin proteins and disrupts their binding to client proteins like cyclin d1 . Numerous cancers overexpress the cyclin d1 gene. The protein, cyclin d1, is an important cell cycle regulator but the role of cyclin d1 in oncogenesis may be independent of cell cycle regulation. We demonstrate in two ovarian cancer cell lines, upon SHetA2 treatment there is a reduction in cyclin D1 protein levels, and upon Olaparib treatment there is minimal effect on total levels. Filamin A promotes tumor metastasis through a variety of signaling molecules when localized to the plasma membrane. Filamin A is widely known as a vital scaffolding protein that is important for cell adhesion and migration. In a cell, Filamin A can promote tumor growth by interacting with signaling molecules, including cyclin D1. After SHetA2 treatment, there was a decrease in colocalization of cyclin d1 with filamin A. Similar trends were seen after Olaparib treatment. Our objective was to evaluate the mechanisms in which the novel drug, SHetA2, alone compares to the front-line competitor, Olaparib, in affecting Filamin A and cyclin D1 levels in ovarian cancer.

EXPLORING THE ROLE OF THE OBESITY-ASSOCIATED EXTRACELLULAR MATRIX IN LOCAL BREAST CANCER PROGRESSION

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Breast cancer is the most prevalent invasive cancer in women. Obesity is a key risk factor implicated in the progression of ductal carcinoma in situ (DCIS) to invasive ductal carcinoma (IDC). Importantly, while breast cancer is often diagnosed as DCIS, it is unknown which lesions will progress to potentially lethal IDC, especially in obesity. The lack of relevant *in vitro* models hinders a mechanistic understanding of obesity's impact on early disease stages when cancer cells invade the local environment. In a retrospective study on human breast specimens, we analyzed gene expression in DCIS and IDC from women with varying BMI. IDC from women with low BMI resembled DCIS from women with high BMI, suggesting tumor-intrinsic effects of obesity on cancer stage. Gene expression profiles highlighted extracellular matrix (ECM) remodeling and epithelial-to-mesenchymal transition pathways in obesity associated DCIS compared to other specimens. We hypothesize that tumor extrinsic mechanisms, particularly ECM alterations, promote DCIS progression in obesity. We developed a novel 3D in vitro model by isolating adipose ECM from lean and obese environments. Human breast cancer cells were cultured in this ECM, and spheroid size, growth rates and number of spheroids were analyzed. We performed untargeted mass spectrometry to define the matrix proteome and pathway analysis of enriched networks in lean and obese conditions. Immunoblot assessed cellular changes in cancer associated signaling molecules. Preliminary findings showed significantly increased number of spheroids and greater breast cancer cell sphere size in obese ECM after three days, indicating an obesity-driven ECM shift that fosters proliferation. Cancer cells in obese, but not lean ECM displayed morphological features of invasion. Our study highlights a crucial role for obesity-induced ECM remodeling in DCIS to IDC transition and in the growth of aggressive breast cancer cells, suggesting therapeutic potential for targeting ECM in obese breast cancer patients with obesity.

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EVALUATING THE EFFECT OF NNT-AS1 MEDIATED REGULATION OF NNT IN PROGRESSION OF HIGH GRADE SEROUS OVARIAN CANCER

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High grade serous ovarian cancer accounts for more than 80% of advanced stage ovarian cancer and 70% of ovarian cancer-related deaths. TCGA data mining of ovarian cancer data revealed frequent amplification of 5p13.2 locus which encodes for NNT-AS1. In agreement with this observation, high expression of NNT-AS1 is observed in ovarian tumors compared to normal ovarian epithelium. Furthermore, the high expression of NNT-AS1 positively correlated with the expression of NNT in tumors and HGSOC cell lines. NNT is critical for producing NADPH that fuels nucleotide synthesis and depletes reactive oxygen levels (ROS). LncRNAs are known to regulate the neighboring genes; hence, to assess the effect of NNT-AS1 on neighboring genes, we evaluated their expression in NNT-AS1-silenced ovarian cancer cells. Our result showed decreased NNT expression while the expression of other genes remains unchanged, implying a potential role for NNT-AS1 in regulating NNT mRNA. Further, treatment of cells with actinomycin D, a known inhibitor of mRNA synthesis, leads to lower expression of NNT in NNT-AS1 silenced cells, confirming the role of NNT-AS1 in stabilizing NNT mRNA.

To assess the potential of NNT-AS1/NNT to drive tumor progression, we assessed cancer cell-innate phenotypic properties of high proliferation, invasion, and migration in cells transfected with NNT-AS1 or NNT. The results showed decreased proliferative, invasive and migratory capacity in NNT-AS1 or NNT silenced OVCAR4 cells. Moreover, silencing of NNT-AS1 or NNT lead to higher ROS and concomitant increase of caspase activity. Finally, we observed an increase in NNT and NNT-AS1 in spheroid culture compared to monolayer culture of ovarian cancer cells, suggesting their potential role in metastasis. Corroborating this observation, we observed expression of NNT correlating with tumor progression with the highest expression in metastatic tumors.

Conclusion: NNT-AS1 is upregulated in ovarian cancer cells and functions as a tumor promoter by stabilizing NNT-mRNA; hence, targeting NNT-AS1 could be a good approach in selectively impeding NNT expression to suppress tumor progression.

MINORITY STRESS CORRELATES OF TOBACCO PRODUCT USE AMONG SEXUAL MINORITY ADULTS IN OKLAHOMA

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Introduction: Tobacco use is the leading cause of cancer and preventable death among U.S. adults. Tobacco use rates are particularly high among sexual minority- (SM; i.e., lesbian/gay, bisexual, or another non-heterosexual identity) relative to heterosexual-identifying individuals. Research is needed to identify individual- and community-level minority stress correlates of tobacco use among SM adults, particularly in states with high structural stigma, like Oklahoma.
Methods: Data were from a survey of 430 SM-identifying adults (ages 18+) residing in Oklahoma, including 291 females (67.7%) and 139 males (32.3%). Participants reported on minority stress experiences (i.e., discrimination, internalized stigma, community acceptance/safety, time spent in LGBTQ+ spaces), current depression and anxiety symptoms, and tobacco use outcomes (i.e., past 30-day cigarette, e-cigarette, other tobacco product [OTP; i.e., cigars, hookah, smokeless tobacco, etc.] use, total number of tobacco products used). Multivariable regressions examined associations among minority stress experiences with tobacco use outcomes controlling for age, race/ethnicity, income, and mental health concerns among females and males, separately.
Results: Among SM females (M_{age}=30.16, 37.5% racial/ethnic minority), discrimination was associated with higher odds of OTP use (aOR=1.08, 95% CI=1.02-1.14) and using more tobacco products (B=0.03, SE=0.01). Among SM males (M_{age}=36.34, 34.5% racial/ethnic minority), discrimination was associated with higher odds of e-cigarette use (aOR=1.07, 95% CI=1.01-1.14), OTP use (aOR=1.13, 95% CI=1.05-1.21), and using more tobacco products (B=0.06, SE=0.02) and internalized stigma was associated with higher odds of cigarette use (aOR=1.73, 95% CI=1.04-2.89) and using more tobacco products (B=0.43, SE=0.17).
Conclusion:Discrimination and internalized stigma were key correlates of tobacco use across a range of products in SM males(i.e., e-cigarette, OTP use, and use of more tobacco products), in SM females however, discrimination was associated only with tobacco products that are less commonly used (i.e., OTP use) and more problematic use (i.e., use of more tobacco products). Tobacco prevention and intervention efforts for SM males in high-stigma environments should incorporate strategies for coping with discrimination and internalized stigma while also attending to the unjust social conditions that perpetuate such stigma. Future research should

consider other factors not assessed here (i.e., tobacco-related norms and, targeted marketing efforts).

PIOGLITAZONE STIMULATES ADIPOCYTE PROGENITOR EXPANSION AND IMPROVES GLUCOSE TOLERANCE DURING BREAST CANCER THERAPY

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The survival rates of women with estrogen receptor-positive (ER+) breast cancer are typically higher when compared to those with ER-negative and triple-negative (TN) breast cancers. This remarkable progress in survivorship during past decades can be attributed to advancements in treatment and enhanced early detection. However, the prevalence of weight gain and increased risk (30%) of type 2 diabetes (T2D) have been observed in breast cancer survivors treated with tamoxifen (TAM) or aromatase inhibitors, particularly in women with elevated BMI. Furthermore, the T2D risk is 19% higher in tamoxifen-treated women compared to matched individuals without cancer, suggesting a potential association between endocrine therapy and diabetes in breast cancer survivors. Our recent research determined that in female obese mice, endocrine therapy disrupted metabolic homeostasis causing glucose intolerance and ectopic fat deposition associated with adipocyte hypertrophy and depletion of adipocyte progenitor cells. We hypothesized that ER signaling maintains adipocyte progenitors to promote healthy adipose expansion during weight gain, which is disrupted with endocrine therapy. Supplementation of pioglitazone, a thiazolidinedione class of drug and agonist for the peroxisome proliferator-activated receptor-γ to endocrine therapy-treated mice promoted proliferation of the adipocyte precursor population within two weeks of treatment. Though pioglitazone did not significantly affect body weight, its protective effect over endocrine therapy was reflected in maintaining estrogen receptor expression, improved insulin sensitivity, reduced subcutaneous adipocyte diameter, decreased visceral fat, diminished liver triglycerides, and less hepatic steatosis. Flow cytometry analysis with mouse adipocyte precursor cells showed that progenitors were greater with either estrogen or pioglitazone treatment and lower after ER antagonism. The loss of progenitor phenotype in endocrine therapy-treated cells was rescued by pioglitazone intervention. The results of this study may help us better understand and prevent the risk for diabetes in breast cancer survivors.

CHARACTERIZATION OF CUTANEOUS PTCL-NOS USING A NATIONAL CANCER DATABASE

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Peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS) is a rare group of non-Hodgkin lymphomas that can originate in a variety of organ systems ranging from the central nervous system to integument and has been associated with poor outcomes. Cutaneous PTCL has been noted to be particularly aggressive with swift disease progression. This study aims to characterize the outcome of patients with cutaneous PTCL-NOS using a national cancer database, particularly in comparison to patients with nodal disease involving the lymph nodes and spleen.

Patients diagnosed with PTCL-NOS between 1975 and 2018 were identified in the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database. Baseline patient and disease characteristics were extracted, and patients were divided into groups based on the primary disease site identified in SEER. Patients with primary disease sites of the skin were placed into a "Skin" group while patients with nodal disease involving the lymph nodes and spleen were placed in a separate group for comparison. Other disease sites were identified and categorized accordingly. Analysis was performed using summary statistics and the Kaplan Meier method. Univariate and multivariate analyses were performed using Cox proportional-hazards models to isolate the effect of primary disease site on both overall survival and lymphoma-specific survival using nodal disease as a comparison group. A 95% confidence interval and p-value < 0.05 were used to determine statistical significance. While our initial analysis included all stages of PTCL-NOS (Ann Arbor stage I-IV), our final multivariate analysis focused on early-stage (I-II) disease as interactions between advanced stage and primary disease site were identified.

3095 patients with PTCL-NOS were identified within the SEER database. The most common primary disease sites were lymph nodes and spleen (67.2%) with skin as the second most common disease site (14.3%). The median overall survival for cutaneous

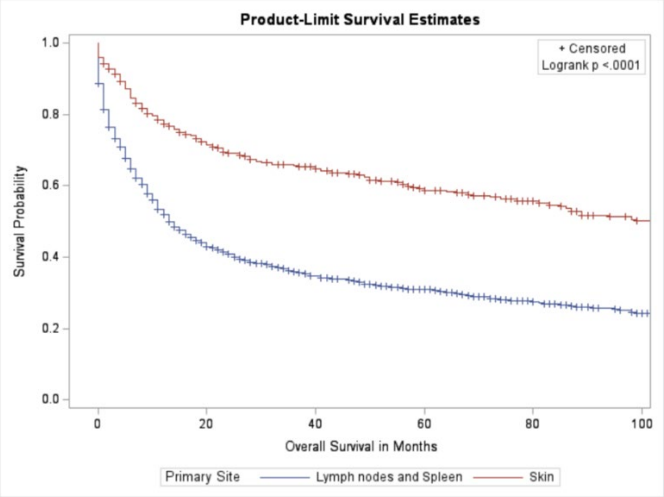
PTCL-NOS of any stage was 115 months (87 to 143) while the median overall survival for PTCL-NOS of the lymph nodes or spleen was 13 months (12 to 15). Similarly, early-stage PTCL-NOS of the skin had increased median overall survival at 202 months (140 to 300) compared to early-stage disease of the lymph nodes or spleen at 47 months (34 to 66). Patients with early-stage PTCL-NOS of the skin had improved overall survival compared to their nodal counterparts (hazards ratio = 0.46, [CI] 0.36 to 0.57, p<0.001). This relationship remained statistically significant after adjusting for confounding variables like age and stage (hazards ratio = 0.54, [CI] 0.42 to 0.68, p<0.001). Lymphoma-specific survival was also improved for early-stage PTCL-NOS of the skin (hazards ratio = 0.39, [CI] 0.28 to 0.53, p<0.001). While overall survival and lymphoma-specific survival were improved for our cohort of patients with PTCL-NOS of the skin, additional studies are needed to further characterize patient outcomes to guide clinical decisions.

Table 1. Cutaneous PTCL-NOS patient characteristics (all stages)

Covariate	Median (SD) or Number (%)
Age (year):	67.0 (13.5)
Under 45	85 (19.3)
45-64	149 (33.8)
65-84	168 (38.1)
85+	39 (8.8)
Stage:	
Stage I	216 (49.0)
Stage II	20 (4.5)
Stage III	15 (3.4)
Stage IV	76 (17.2)
Unknown	114 (25.9)
Race:	
Non-Hispanic White	334 (75.7)
Non-Hispanic Black	50 (11.3)
Non-Hispanic Asian/Pacific islander	23 (5.2)
Hispanic	23 (5.2)
Non-Hispanic American Indian/Alaskan Native	5 (1.1)
Unknown	6 (1.4)
Sex:	
Female	180 (40.8)
Male	261 (59.2)
Chemotherapy	
Yes	152 (34.5)
No/Unknown	289 (65.5)
Radiation	
Yes	127 (28.8)
No/Unknown	314 (71.2)
Surgery	
Yes	140 (31.7)
No/Unknown	301 (68.3)

SD indicates standard deviation.

Figure 1: Kaplan-Meier: All stage (Stage I-IV) cutaneous and nodal PTCL-NOS 8-year survival



ROLE OF CBS IN DIFFERENT CELL TYPES OF OVARIAN CANCER TUMOR MICROENVIRONMENT

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Background: Ovarian cancer (OC), a leading cause of gynecologic cancer death, is characterized by high expression of Cystathionine beta-synthase (CBS), a sulphur amino acid metabolizing enzyme, promoting tumor growth and metastasis. Our team has previously identified CBS as a potential therapeutic target for relapsed and drug-resistant OC, demonstrating its significant positive effects on OC cell proliferation and metastasis. CBS modulates redox balance and metabolism of OC cells, including elevated lipid metabolism, an observation associated with poor survival. Given CBS's importance in OC cell survival, and since molecules secreted by cancer-associated fibroblasts (CAFs) and endothelial cells (ECs) in the tumor microenvironment (TME) are known to aid cancer cell (CC) survival in OC, it's crucial to look into the potential role of CBS in the survival and functioning of these cell types in TME too.

Hypothesis: Since CBS's crucial role in ovarian CC function, we hypothesize that modulating CBS in other tumor microenvironment (TME) cell types could effectively hinder their function and attenuate overall tumor progression.

Methodology: Our study focuses on three cell types' viz. OC cells, CAFS and ECs for which we have used OVCAR 4 or OVCAR 8, CAF 19 and HMEC cells respectively and have investigated how the interaction and functioning of CC-CAFs-ECs are affected by knocking down CBS in each cell type. This involved conducting wound healing migration assays in OVCAR 8, CAF 19 and HMEC cells following siRNA mediated CBS knockdown and 3D culture to assess spheroid formation by OVCAR 4 with stable CBS shRNA expression. Additionally, we examined the expression of sulfur metabolism enzymes (CSE and MPST) and epithelial-mesenchymal transition (EMT) markers in each cell type following CBS knockdown.

Result: CBS knockdown impeded migratory potential in all three cell lines, as observed in scratch assays. In HMEC, this outcome associated with pVEGFR-2 downregulation. Meanwhile, in CAF 19 and OVCAR 8, CBS knockdown led to Snail downregulation, a key transcription factor in epithelial-mesenchymal transition (EMT). CSE and MPST remained unaffected by CBS knockdown. Spheroid formation assays showed reduced size in CBS-knocked down OVCAR 4 cells. Notably, EMT factors like Snail and Twist were also downregulated in CBS-depleted 3D spheroids.

Conclusion: Overall, these results indicate CBS's vital role in these TME cell types. We further aim to unravel how CBS knockdown in one cell type can modulate the functioning of other through co-culture experiments.

NON-NECROPTOTIC ROLES OF MLKL IN DIET-INDUCED OBESITY, LIVER PATHOLOGY, AND INSULIN SENSITIVITY

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Metabolic disorders such as obesity and type 2 diabetes are major risk factors for metabolic dysfunction-associated fatty liver disease (MAFLD) that impacts 20-30% of the US population. Nearly 25% of individuals with MAFLD develop metabolic dysfunction-associated steatohepatitis (MASH), a condition linked to considerable morbidity and mortality. Chronic inflammation has been identified as a key player in MAFLD and its progression to liver cirrhosis and liver cancer. Necroptosis, an inflammatory cell death pathway, is elevated in MAFLD patients and mouse models, yet the role of necroptosis in MAFLD is unclear due to diverse mouse models and inhibition strategies. In our study, we inhibited necroptosis by targeting mixed lineage kinase domain like pseudokinase (MLKL), the terminal effector of necroptosis, in a high-fat, high-fructose, high-cholesterol (HFHFrHC) mouse model of MAFLD. Despite HFHFrHC diet upregulating MLKL (2.5-fold), WT mice livers showed no increase in necroptosis markers or associated proinflammatory cytokines. Surprisingly, *Mlkl*$^{-/-}$ mice experienced exacerbated liver inflammation without protection from diet-induced liver damage, steatosis, or fibrosis. In contrast, *Mlkl*$^{+/-}$ mice showed significant reduction in these parameters that was associated with elevated Pparα and Pparγ levels. Both *Mlkl*$^{-/-}$ and *Mlkl*$^{+/-}$ mice on HFHFrHC diet resisted diet-induced obesity, attributed to increased beiging, enhanced oxygen consumption and energy expenditure due to adipose tissue, and exhibited improved insulin sensitivity. These findings highlight the tissue specific, non-necroptotic effects of MLKL on the liver and adipose tissue, and suggest a dose-dependent effect of MLKL on liver pathology.

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CANCER CELL PLASTICITY DRIVEN BY CLINICAL THERAPY PRESSURE

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Intra-patient heterogeneity in known driver molecules pre- and post-intensive multimodal clinical therapy is known to associate cancer progression. Such heterogeneity is known to prompt cancer cell adaptation and plasticity, particularly lineage transformation and cancer stem cell (CSC) clonal expansion. Herein, we investigated the acquired plasticity of neuroblastoma (NB, predominant extracranial solid cancer in infants) tumor cells with therapy pressure, and the mode of action. Bed-to-bench strategy utilizing cells derived during diagnosis (Dx) and progressive disease (PD, tumors that defy chemoradiotherapy, stem cell transplantation, immunotherapy etc.) from patients with stage-4 NB were assessed for plasticity and lineage transformation. Compared to the clones derived during Dx, we observed a significant increase in the expansion of CD133+CD114+CD117-, CD133-CD114+CD117+ and CD133+CD114-CD117+ NB-CSCs in PD clones (FACS sorting with stringent inclusion exclusion strategy). Further, PD clones (vs. Dx) exhibited profound modification in the drivers of differentiation (GAP43, β3-Tubulin, GFAP, NF-L), EMT (E-Cad, N-Cad, Vimentin, SLUG), stemness maintenance (SOX-2, OCT3/4, NANOG, CD54, NOTCH1) and, motility related (RON-β, MMP-9, MMP-2) drivers (immunoblotting). These PD clones accrued high metastatic state (invasion and migratory capabilities). Crucially, PD clones exhibited a significant transcriptional (qPCR) and translational (immunoblotting, ELISA) loss of retinal degeneration protein 3 (RD3). More importantly CSC-related proteome profiling in reverse engineered RD3-Dx clones (stable RD3 knockout) recognized RD3-dependent regulation of EMT, stemness maintenance and CSC self-renewal drivers. Together, the results portray the acquired plasticity of NB cells, and further depict that the de novo acquisition of RD3 loss prompts the therapy pressure acquired RD3 loss mediates the NB $\rightarrow$CSC lineage transformation. This new information allows us to move forward developing new, effective tumor-targeted, molecular-targeted maintenance therapeutic strategy for therapy resistant progressive tumors.

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THE ROLE OF NECROPTOSIS-ASSOCIATED CHRONIC INFLAMMATION IN THE DEVELOPMENT OF LIVER CANCER IN NOVEL KNOCK-IN MOUSE MODELS FED A WESTERN DIET

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Non-resolving chronic inflammation is a major contributor to aging as well as the etiology of many age-related diseases, including cancer. Necroptosis is a pathway of regulated necrosis involving the Ripk3 and Mlkl genes and plays a major role in inflammation. We have shown that necroptosis increases with age in several tissues. Pharmacologically/genetically blocking necroptosis reduces inflammation in several diseases as well as aging. The severity of inflammation is closely correlated with the incidence of chronic liver diseases (CLD) and liver cancer, especially in response to high-fat feeding and obesity. The goal of this research project is to use novel-knock-in mouse models, which we have generated, to directly test the role of hepatic necroptosis induced inflammation in mice fed a western diet (WD). Specifically, we are using two novel KI mouse models (*Ripk3-KI* and *Mlkl-KI* mice) that overexpress Ripk3 and Mlkl specifically in hepatocytes when crossed albumin-cre mice, i.e., *hRipk3-KI* and *hMlkl-KI* mice. We hypothesize that overexpressing either Ripk3 or Mlkl in hepatocytes will increase necroptosis and inflammation in the liver, promoting fibrosis, and liver cancer in mice fed WD. To test our hypothesis, we subjected control mice (either *Ripk3-KI* or *Mlkl-KI* mice), *hRipk3-KI* mice, and *hMlkl-KI* mice to WD feeding for 3-, 6-, and 12-months. The control and hepatic KI mice showed similar increases in body weight and eWAT weight. Importantly, we found increased necroptosis in hepatic KI mice models fed a WD compared to control mice on the same diet. Furthermore, we also found elevated levels of pro-inflammatory macrophages (CD68) and inflammatory cytokines (e.g., TNFα, IFNγ, NF-κb, SREB1,2) in hepatic KI mice models fed a WD after 3, 6, and 12 months of feeding compared to control mice fed a WD. The hepatic KI mice show increased fibrosis (hydroxyproline assay, picrosirius red staining) in the livers of the hepatic KI mice compared to control mice fed a WD starting at 6-months of age. There is no evidence of tumor development in the control or hepatic KI mice models fed a standard chow diet. However, 20-30% of the control mice on the WD showed the presence of liver tumors at 12-months of age. In contrast, ~60% hepatic KI mice showed the presence of liver tumors. Further analysis revealed a significant increase in the average number of liver tumor nodules in each liver and a higher incidence of >5mm

sized tumor nodules in the livers of hepatic KI mice compared to control mice. In conclusion, our study demonstrates that necroptosis specifically in hepatocytes can lead to the development of fibrosis and liver cancer in mice fed a WD.

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NOMOGRAM TO PREDICT CLINICALLY SIGNIFICANT DISEASE IN PATIENTS WITH AN ELEVATED PSA AND AN MRI PRIOR TO PROSTATE BIOPSY

Reagan Amason, Robin Djang, Michael Cookson, and Kelly Stratton

Introduction and Objectives: A nomogram-based approach has been shown to accurately predict the outcome of prostate biopsy in men with an elevated PSA using known traditional risk factors. More recently, the benefit of prostate MRI prior to the decision to perform a biopsy has been shown to both reduce unnecessary biopsies and enhance the yield of high grade prostate cancer. This study aimed to predict outcomes of prostate biopsy findings based on combining traditional risk factors with the imaging findings on prostate MRI prior to biopsy. A nomogram was then created to improve accessibility to predicted outcomes and aid in decision making.

Methods: We retrospectively reviewed our prostate biopsy database to identify a cohort of 448 biopsy-naive men who had an elevated PSA, a prostate MRI, and underwent transrectal ultrasound-guided prostate biopsy (TRUS-Bx) were included. Age, race, PSA, prostate volume, PSA density, PIRADS, digital rectal exam (DRE), and Gleason score were evaluated. Significant cancer (csPC) was defined as Gleason Score 7 (3+4) (Grade Group 2) or higher. A high PSAd was defined as > 0.15ng/mL^2. An elevated PSA was defined as >4 ng/mL. A high PIRADS score was defined as score > 3.

Presence of csPC was used as a dichotomous outcome variable in a logistic regression setting. After removing records with missing outcome, logistic models were fit independently for age(years), race (white vs. other), prostate volume (cc), pre-biopsy PSA, adjusted PSA, PSA density, PIRADS score (both in point increase and as a categorical variable compared to a baseline of 1), and presence of abnormal DRE. An adjusted model was built starting with a saturated model containing all individually-significant predictors and relevant interactions with age. Following removal of non-significant interactions, any non-significant main effects not involved in an interaction were removed until all remaining terms were significant. Then, the model was stratified by the median age, and adjusted ORs were computed within each stratum. All analyses were conducted using R v4.3.1 (R Core Team, 2023), and predicted probabilities were used to develop an interactive web app using RShiny, hosted on shinyapps.io; no personally identifiable information was included in the model results or web app for cloud hosting. Model performance was assessed using 10-fold cross validation.

Results:The mean age of the cohort was 65.97 ± 7.74 years, and 81.28% of the cohort were white. The mean PSA of the men was 12.60 ± 13.04 ng/mL. In total, 7% were found to have abnormal DRE. The mean prostate volume was 58.92 ± 38.46 cc. The mean PSAd of the cohort was 0.27 ± 0.30 ng/mL^2, with 98.6% falling under that threshold. 289 (65%) men were found to harbor a high PIRADS score. The following was the breakdown of PIRADS score among

participants PIRADS score ≤3 (35%), PIRADS 3 (20%) PIRADS 4 (27%) PIRADS 5 (17%). Of the 448 men, 36% were diagnosed with csPC.
A significant ($p<0.0001$)interaction with age was found, so stratified models were developed for patients up to 66 years of age, vs. patients older than 66 years. After stratification, the final model included terms for prostate volume, PSA, and PIRADS score treated as a numeric predictor (i.e., the OR was computed per each 1-point increase) . The results of the analyses used to develop the nomogram are displayed in table 1. The model achieved 82% AUC, with 60.9% sensitivity, 81.49% sensitivity, and 73.7% overall accuracy.
Table 1: Modeling results

Patient subset	Predictor	Contrast	Odds Ratio (OR)	95% LCL	95% UCL	p-value
Age ≤ 66	Prostate volume	(1-cc increase)	0.9864	0.9769	0.9950	0.0034
	PSA (Pre)	(1-unit increase)	1.0122	0.9875	1.0435	0.3832
	PIRADS	(1-point increase)	2.1858	1.6697	2.9227	<0.0001
Age > 66	Prostate volume	(1-cc increase)	0.9556	0.9297	0.9765	0.0003
	PSA (Pre)	(1-unit increase)	1.0724	1.0126	1.1488	0.0345
	PIRADS	(1-point increase)	2.7816	1.9291	4.1749	0.0000

Conclusion:The nomogram is intended to be used in scenarios where a patient with an elevated PSA and an MRI of the prostate is being evaluated for csPC prior to biopsy. However, the nomogram will be specifically useful in discussions where a patient has borderline parameters where the provider is uncertain if a biopsy is needed. In our cohort, age, PSA, prostate volume, and PIRADS were the most significant factors in predicting csPC on biopsy. The nomogram

combines the significant traditional risk factors with MRI findings to provide a powerful prediction of clinically significant prostate cancer in biopsy-naive men.

INHIBITION OF OVARIAN CANCER PROLIFERATION: TARGETING OXYSTEROL-BINDING PROTEINS AND INTRACELLULAR LIPID TRANSPORT

Richard Bui, Jorge L Berrios Rivera, Susan L Nimmo, Anthony W. G. Burgett

"Ovarian cancer's late-stage diagnosis and resistance to standard-of-care (SOC) therapies pose significant challenges. We investigate the role of cholesterol and oxysterol-binding proteins (OSBP and ORP4) in the context of ovarian cancer spheroids, which often metastasize in nutrient-poor peritoneal environments.

Prior evidence reveals that serum cholesterol and LDL levels correlate with disease aggressiveness, highlighting the potential significance of cholesterol access in ovarian cancer spheroids. We demonstrate that a compound targeting OSBP/ORP4 exhibits nanomolar anticancer activity against in vitro ovarian cancer spheroids, surpassing the efficacy of SOC drugs like paclitaxel and cisplatin.

OSBP regulates intracellular cholesterol movement and is hypothesized to act as an overall lipid sensor, while ORP4's function remains elusive but is highly expressed in ovarian cancer. We propose that disrupting cholesterol transport and usage may exploit the sensitivity of ovarian cancer spheroids, as evidenced by lipid depletion and statin-cholesterol biosynthesis blocking, enhancing the anticancer activity of OSBP/ORP4 targeting natural compound OSW-1, but not SOC drugs.

Our findings support the potential development of OSBP-specific and ORP4-specific compounds, offering insights into these intriguing targets. This research opens doors to precision cancer treatments and a deeper understanding of cholesterol-related mechanisms in ovarian cancer."

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CELL-SPECIFIC TRANSGENIC MOUSE MODEL OF SOLID CANCERS: NEUROBLASTOMA AND BEYOND

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Neuroblastoma is a neural crest cell (NCC) derived pediatric tumor accounting to about 6-10% of all childhood cancer cases. Our sequential studies showed that Retinal Degeneration Protein 3 (RD3), a regulator of photoreceptor cell survival, is available in all tissues beyond retina and, is required for the regulation of tumor pathogenesis. Here in, we investigated whether cell-specific RD3-loss instigates tumorigenesis. For this, we designed a versatile RD3 LoxP mice that could be used for multifarious solid tumor models with cell-specific RD3 conditional knockout (KO)strategy. Here in we utilized NCCs-specific Cre combination targeting tyrosine hydroxylase (TH-Cre, that was developed in house in A129 background to match RD3-LoxP background) coupled with ROSA26 GNZ knock-in (that express nuclear-localized GFP/β-gal fusion protein when an upstream loxP-flanked STOP sequence is removed) to generate NCC-specific RD3-KO mice. NCC-specific RD3-KO was validated in E9.2 by assessing (automated IHC) for the localization and expression of RD3, and NCC markers including TH, SOX9, SYP, ENO2, and VIM. RD3-loss in NCC derived tissues including adrenal, spinal cord, brown-adipose tissue were confirmed in young adults (confocal imaging for GFP/RFP) and compared with non-NCC derived tissues (lung, liver, kidney etc.) Equally balanced (male-female) RD3-KO homozygous mice were continuously monitored up to 500 days for the generation of spontaneous tumor development. Strikingly, NCC-specific RD3-KO instigates spontaneous tumor formation (in liver, SI, abdomen etc.) as early as 24 days, but varied greatly (20days through 426 days). NB phenotype was confirmed histologically by the pediatric pathologist and with the combined expression profile of NB specific ENO2, TH, and SYP. These results clearly portray a cell-specific RD3-KO results in spontaneous tumorigenesis and implies that RD3-loss as the driver for tumor initiation. More importantly, NCC-specific RD3 knock out definitively instigates NB. These outcomes, for the first time provide a preclinical platform for investigating tumor progression and evolution in neuroblastoma and could be extrapolated to other tumors with cell-specific strategies.

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UNDERSTANDING THE LINK BETWEEN INFLAMMATION, NECROPTOSIS, AND AGING LIVER: IMPLICATIONS FOR NONALCOHOLIC FATTY LIVER DISEASE AND HEPATOCELLULAR CARCINOMA

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Chronic inflammation significantly contributes to both the initiation and advancement of hepatocellular carcinoma (HCC) and plays a pivotal role in the development of non-alcoholic fatty liver disease (NAFLD) linked to obesity—a prominent risk factor for HCC in the United States. HCC exhibits heightened prevalence in the elderly, predisposing them to increased mortality. Despite the well-established connection between inflammation, aging, and HCC, the precise molecular processes governing inflammation and its role in age-related HCC remain unclear. We hypothesized that necroptosis, an inflammatory mode of cell death, plays a contributory role in age-related hepatic inflammation and the development of HCC associated with NAFLD in mice. Our studies in *Sod1*$^{-/-}$ mice, a model of accelerated aging and spontaneous HCC development, show the pharmacological inhibition of necroptosis attenuated necroptosis, inflammation, and fibrosis in the liver. Similarly, genetic (*Ripk3*$^{-/-}$ and *Mlkl*$^{-/-}$ mice) and pharmacological (Necrostatin-1s) blocking of necroptosis resulted in reduced hepatic inflammation (TNFα, IL6, IL1β, CCL2), pro-inflammatory M1 macrophages, senescence markers (p16, p21) and features of NAFLD (fibrosis, steatosis). In a direct investigation of necroptosis in NAFLD-induced HCC, both control (WT) mice and those lacking *Ripk3* or *Mlkl* were given an HCC-inducing diet. Compared to control mice, *Ripk3*$^{-/-}$ and *Mlkl*$^{-/-}$ mice showed decreased hepatic inflammation, pro-inflammatory macrophages, tumor incidence, and expression of oncogenic proteins. Additionally, *in vitro* experiments revealed inhibition of necroptosis, achieved through either necrosulfonamide treatment or siRNA, resulted in reduced cell proliferation and colony formation ability in human liver cancer cells. In conclusion, our findings indicate the critical involvement of necroptosis as an inflammatory mediator in both aging and HCC. This implies that targeting of necroptosis could serve as a potential approach to prevent HCC development in the elderly.

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ADVANCING PRECISION ONCOLOGY: HARNESSING ANNEXIN A5-MEDIATED DRUG DELIVERY FOR ENHANCED CHEMOTHERAPY IN TRIPLE-NEGATIVE BREAST CANCER

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Triple-negative breast cancer (TNBC) remains a formidable clinical challenge, necessitating innovative solutions for improved therapeutic efficacy and diminished adverse effects. In this study, we introduce a therapeutic strategy designed to optimize chemotherapy delivery to the tumor microenvironment, taking in account the external exposure of phosphatidylserine (PS) on TNBC cells.

Our approach involves the precise targeting of PS expression through its binding partner, annexin A5 (ANXA5). Mertansine (DM1), a potent chemotherapeutic agent, is conjugated to ANXA5, forming ANXA5-DM1 with a drug: protein loading ratio of 4:1. Functioning as a tailored delivery vehicle, ANXA5 facilitates the directed delivery of DM1 to TNBC cells, exploiting the specific PS expression pattern.

Experimental findings on two distinct mouse TNBC cell lines underscore the remarkable efficacy of ANXA5-DM1, exhibiting toxicity levels surpassing free DM1 by over two orders of magnitude. Notably, ANXA5-DM1 demonstrates a safety profile at least three orders of magnitude superior to healthy mammary cells compared to TNBC cells. Furthermore, the study sheds light on the immunogenic cell death induction facilitated by ANXA5-DM1.

Critical insights reveal that DM1, when administered in isolation, imparts notable toxicity to healthy cells; however, when strategically conjugated with annexin A5, its cytotoxic impact is significantly attenuated. Importantly, annexin A5 exhibits an inherent selectivity, binding effectively to TNBC cells while sparing healthy counterparts.

In summation, our research advocates for the potential paradigm shift offered by ANXA5-DM1, presenting a targeted therapeutic strategy for TNBC. This innovation addresses the imperative for enhanced chemotherapy precision and reduced off-target effects, positioning itself as a promising advancement in the realm of TNBC treatment modalities.

NOVEL, ENGINEERED FUSOGENIC LIPOSOME-BASED ANTI-OXIDANT DELIVERY SYSTEM IMPROVES THE BLOOD-BRAIN BARRIER INTEGRITY IN AGING

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Vascular dysfunction plays a pivotal role in age-related cognitive decline and neurodegeneration. The aging process often leads to a loss of integrity in the blood-brain barrier (BBB), initiating neuroinflammation and contributing to a decline in cognitive function. In previous research, we demonstrated the potential of resveratrol (RSV), a natural polyphenol, to target cerebromicrovascular endothelial cells (CMVECs), effectively countering age-related oxidative stress and improving vascular function, both in vitro and in vivo. However, the limited bioavailability of resveratrol raised questions about its effectiveness concerning the BBB and neuroinflammation.

Our study aimed to address this challenge by introducing a novel drug delivery system designed to enhance the efficiency of polyphenol delivery. This innovative approach involved the use of fusogenic liposomes (FL) integrated with a bioengineered protein corona (PC) featuring specific apolipoprotein E (ApoE). Our central hypothesis posited that PC formation could be harnessed to directly target CMVECs and enhance liposomal uptake, with the ultimate objective of effectively delivering RSV to the brain's microvessels in aging subjects (ApoE-FL-RSV).

Our investigation encompassed the characterization of ApoE-FL uptake by CMVECs, along with an analysis of its biodistribution and pharmacokinetics in vivo. Remarkably, our findings revealed a significant increase in ApoE-FL-RSV accumulation within CMVECs in vivo, compared to control FL uptake. We employed advanced in vivo multiphoton imaging to longitudinally monitor the effects of ApoE-FL-RSV on the BBB, which demonstrated a significant rejuvenation of the endothelial barrier function in aged mice treated with ApoE-FL-RSV.

In light of these results, we concluded that the fusogenic liposomal delivery system holds promise as a viable pharmacological intervention for addressing age-related vascular cognitive impairment.

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EPIDEMIOLOGY, CLINICAL CHARACTERISTICS, AND TREATMENT STRATEGIES OF POLYMORPHOUS ADENOCARCINOMA OF THE HEAD AND NECK

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Introduction: Polymorphous Adenocarcinoma (PAC) is a rare malignant head and neck neoplasm that is heterogenous in histopathological appearance and clinically unpredictable. Because of its relatively low incidence, there remains a paucity of data regarding the optimal treatment algorithm of this disease process. The objective of this study is to update the epidemiology, clinical characteristics, and treatment strategies of PAC with the use of a large national database.
Methods: The Surveillance, Epidemiology, and End Results (SEER) database was queried for all cases of PAC from 2001 to 2019.
Results: 756 cases of PAC were included for statistical analysis with the mean age at diagnosis being 61.6 years $\pm$ 14.2, and a predominance of females at 68.7%. 74.5% were considered early stage at diagnosis, and 25.5% were considered late stage. Mean survival time was significantly greater for patients with early-stage disease (152 months [95% CI, 145-160]) than for those with late-stage disease (129 months [95% CI, 114-144], $p = 0.003$). Treatment data demonstrated a significant survival benefit for the mean survival time of those who underwent surgery (89.2%) (174 months [95% CI, 167-181]) as compared to those who did not receive surgical treatment (111 months ([95% CI, 89-132], $p < 0.001$. Overall, 5-year survival was noted to be 86%.
Conclusion: This study includes the treatment outcomes and clinical characteristics of PAC from a large national database and provides data from the largest and most contemporary cohort. Treatment with surgery and female sex were independent predictors of survival time, with early stage corresponding to increased survival. Overall, patients in this study had an excellent prognosis.

EVALUATING THE FUNCTIONAL ROLE OF HISTONE ACETYLTRANSFERASES IN GLIOBLASTOMA RESISTANCE

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Glioblastoma (GBM) is a highly aggressive and malignant primary adult brain tumor with poor prognosis. The current standard treatments of GBM such as fractionated radiation and chemotherapy with Temozolomide fail to impede tumor recurrence. Treatment failure is primarily attributed to glioma stem-like cells (GSC) and a fraction of non-stem tumor cells that acquire phenotypic plasticity and develop resistance. Epigenetic modifications play a vital role in promoting phenotypic plasticity and therapeutic resistance. Histone Acetyltransferases (HATs) are enzymes that acetylate histone and non-histone proteins to modulate gene expression and regulate various cellular processes including proliferation, differentiation and DNA repair. However, the functional role of HATs in mediating GBM resistance is poorly understood. Here, we performed a small molecule inhibitor screening to investigate the effects of HAT inhibition on GBM growth and radiation resistance. We first determined the IC50 of HAT inhibitors and validated their inhibitory effects on histone acetylation. Our findings indicate that HAT inhibition significantly reduced the viability and proliferation of patient-derived GBM cell lines. Furthermore, HAT inhibition also decreased glioma stem cell marker expression and sensitized GBM cells to radiation-induced DNA damage. Ongoing experiments are aimed at determining the molecular mechanisms by which HATs promote GBM resistance.

RD3 REGULATES DE NOVO FORMATION OF MUSCLE INVASIVE DISEASE FROM NON-MUSCLE INVASIVE BLADDER CANCER

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Non-muscle invasive bladder cancer (NMIBC) is a heterogeneous type of urothelial carcinoma with a substantial risk (>50%) of tumor progression and muscle invasion. Our sequential studies uniquely unveiled the availability of Retinal Degeneration Protein 3 (RD3) in human adult/fetal tissues and recognized its functional significance in tumor evolution. Herein, we investigated the relevance of RD3 in coordinating de novo MIBC from NMIBC. Compared to the low grade tumor, RD3 is significantly lost (mRNA, qPCR; protein, ELISA) in grade III and IV patient derived NMIBC cells.In a cohort of (n=55) NMIBC patients, RD3-loss associated with increased tumor invasive potential (complete loss in highly invasive T4), metastasis (vs. primary tumors), therapy pressure (insignificant levels in progressive disease that defies therapy), disease recurrence, and death (custom archived TMA with automated RD3 IHC).Crucially, we observed a significant low-is-worse association to overall survival (p=7.30E-03, hazard ratio (HR) of 5.161), relapse-free survival (p=4.464E-02, HR = 2.328), and progression-free survival (p=7.00E-0.4, HR = 3.264). Further, radio-resistant cells exposed to fractionated irradiation (FIR, 2Gy/Day for 5 days) to a total dose of 10 or 20Gy displayed a dose dependent loss of RD3 recognizing an ongoing acquisition of RD3-loss with therapy pressure. More interestingly, Grade I or III bystander cells (BSE) co-cultured with FIR-exposed cells displayed anew acquisition of RD3-loss and displayed tumor grade-dependent increase (vs. mock-irradiated) in NFκB transcriptional activity (EMSA) and the activation of NFκB trans-activated pro-survival molecules (QPCR profiling of 89 NFκB targets). Together, these results clearly depict that RD3 regulates NMIBC disease pathogenesis, dissemination, acquired loss of RD3 with therapy pressure and further implies its role in the evolution of de novo MIBC from NMIBC.

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UNVEILING PRECISION TARGETS: OSBP AND ORP4 IN OVARIAN CANCER THERAPY WITH OSW-1 ANALOG COMPOUNDS

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Ovarian cancer (OC) poses a considerable threat as a highly lethal gynecologic tumor, with over 20,000 new cases diagnosed annually. Given the limited long-term survival rates for OC patients, there is an urgent need for the development of effective and personalized treatment strategies. Our research identifies oxysterol-binding protein (OSBP) and OSBP-related protein 4 (ORP4) as promising targets for precision cancer treatment in OC. OSBP plays multifaceted roles in the lipid transport and viral replication. Conversely, ORP4, while not yet fully understood in terms of its exact mechanisms, is recognized as a significant player in the context of leukemia and cancer cell proliferation. We have demonstrated that the natural compound OSW-1, by targeting OSBP and ORP4, exhibits superior anti-cancer effects against ovarian cancer cell lines, specifically ES-2, compared to conventional chemotherapy drugs like cisplatin and paclitaxel. To enhance the efficacy of targeted therapies, our lab has synthesized analogs of OSW-1. The primary objectives are to comprehensively investigate the underlying mechanisms of these OSW-1 analogs in both 2D and 3D ovarian cancer cell models and to examine the Structure-Activity Relationship (SAR) of OSW-1-related compounds. Encouragingly, initial findings reveal significant anti-cancer effects in both settings, and the SAR with varying side chain modifications, indicates the importance of esterification for the effectiveness. The overarching goal of this research is to understand the role of oxysterol-binding proteins in ovarian cancer growth and to advance compounds targeting these proteins as a novel and precise approach for OC therapies.

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MECHANISMS DETERMINING WHERE DNA REPLICATION INITIATES IN THE HUMAN GENOME

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The selection of replication origins is a defining characteristic of DNA replication in higher eukaryotes, yet its mechanism in humans has not been well-defined. In yeast, origin selection involves replication initiation factor (Sld3-Sld7) recruitment to origins during G1. In this study, we use Cut&Run to examine genomic binding locations for TICRR and MTBP, the Sld3 and Sld7 orthologs. We have constructed two HCT116 human colorectal cancer cell lines in which the endogenous TICRR or MTBP loci were tagged at their carboxy-termini with mClover. Using these cell lines, we have shown that TICRR and MTBP genomic binding sites can be mapped using Cut&Run with anti-GFP antibody. We mapped TICRR and MTBP binding throughout the cell cycle by performing experiments in asynchronous, G1, or G2-arrested cells. Peaks of TICRR and MTBP binding frequently overlap at Ini-seq replication origins. Additionally, our results show HCT116 TICRR and MTBP peaks overlap with MTBP peaks previously defined (Kumagai et al. Cell Rep. 2020) in a DLD-1 cell line. Interestingly, our data show that TICRR and MTBP binding patterns are less defined in asynchronous cells than G1, possibly due to cell cycle phase-specific recruitment of TICRR-MTBP to replication origins in human cells.

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ALLEVIATION OF TUMOR-INDUCED CACHEXIA BY RET-SELECTIVE INHIBITOR SELPERCATINIB

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Background and Objectives: Cancer-associated cachexia is a devastating syndrome characterized by body weight loss, particularly skeletal muscle atrophy. Currently, there is no effective therapy for cancer-associated cachexia. Glial cell derived neurotrophic factor (GDF15) is known to regulate body weight. Recently, GDF15 was found to activate RET protein tyrosine kinase via binding of its co-receptor, GDNF family receptor α-like(GFRAL). In clinical trials of RET-targeted therapy, a side effect of RET-selective protein kinase inhibitors selpercatinib and pralsetinib was body weight gain. Thus, we hypothesize that a RET-selective kinase inhibitor may be used to treat cancer-associated cachexia. In this study, we investigated whether selpercatinib could alleviate cachexia in a tumor model in animals.
Methods: Human Fibrosarcoma (HT-1080) cells were subcutaneously injected into the right flank of ICRSC-F mice to induce cachexia. Mice were divided into three groups, tumor bearing mice treated with vehicle and selpercatinib (30 mg/kg, qd) by oral gavage, and tumor free mice treated with vehicle. Food intake, grip strength, body weight, and tumor size were measured for each group. Endpoint was determined by 20% reduction from primary body weight. Hindlimb muscles, (tibialis anterior (TA), quadriceps (QA) and gastrocnemius (GA)), subcutaneous fat and brown fat were collected, weighed and snap-frozen in liquid nitrogen. Terminal blood was collected by cardiac puncture, and plasma was extracted to measure GDF-15 level in circulation.
Results: HT1080 cells caused significant body weight loss and reduced food intake in both groups compared to the tumor free mice. Human GDF15 based ELISA showed an increased GDF-15 level in circulation of both tumor-bearing mice groups. Both fat loss and muscle loss were observed in the cachectic phenotypes while selpercatinib-treated group showed a significant rescue of fat and muscle loss, improved grip strength and food intake.
Conclusions: The rapidly growing HT1080 tumors caused cachexia in the host mice, characterized by body weight loss, muscle loss, and fat loss, and loss of food consumption. Plasma GDF15 was elevated in mice bearing HT1080 tumors. Selpercatinib at 30 mg/kg/day significantly improved the food consumption, body temperature, grip strength, skeletal muscle weight, and white fat weight of the tumor bearing cachectic animals. These results show that selpercatinib partially alleviated cachexia at the testing dose.

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CANCER-RELATED PATIENT NAVIGATION FOR NATIVE AMERICAN INDIVIDUALS

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Background: The Native American (NA) population of the United States faces significant disparities surrounding many facets of cancer care. NA patients have a high morbidity and mortality related to cancer, with the worst survival rates in the country [1-3]. Additionally, NA patients experience disparities in cancer prevention and receipt of supportive cancer care. For instance, these individuals are significantly less likely to receive hospice care or guideline concordant cancer care making them more susceptible to poor outcomes [4,5]. Prior work has sought to explore attributable factors to address the presence of these disparities. However, relatively little research in implementing interventions to address these factors exists. Patient navigation is described as professional guidance to patients through logistics and supportive care that reaches beyond their treatment [6]. Navigation has recently been recognized by the Centers for Medicare and Medicaid Services as a reimbursable strategy to help improve cancer outcomes. Thus, these programs hold great potential to help address cancer disparities in NA communities. We aim to study the reach and effectiveness of navigation services tailored specifically to the NA population in the United States.

Methods: We used the Ovid MEDLINE database to search literature published on NA navigation programs with no date restrictions, which resulted in 113 publications. Text review was then completed by two or more reviewers, following PRISMA guidelines, using Covidence software. Inclusion criteria for this review were literature describing facets of NA navigation described in the US, with exclusions for texts that generalized minority groups, were conducted outside of the US, and systematic or literature reviews. From this, a total of 16 studies were included in this review.

Results: The available data supports positive or neutral outcomes for NA patients who participated in a navigation program. In two clinical trials, patients undergoing radiation therapy who were enrolled in NA tailored navigation had significantly fewer treatment interruptions

compared to NA patients who did not receive navigation [7,8]. Additionally, navigated NA patients showed higher rates of clinical trial enrollment and preventative cancer screening in comparison to the national average of NA participation [7,9]. When surveyed post-treatment, NA patients who received navigation services reported significantly higher satisfaction with their care experience [9,10].

Conclusions: To reduce disparities and improve patient outcomes among NA patients with cancer, navigation teams must prioritize the cultural values of NA patients to address their unique needs. Unfortunately, despite the progress made, there is still a paucity of literature on NA patient navigation services. The existing literature supports the need for additional research regarding NA patient navigation to determine a generalizable consensus of the effectiveness of this strategy.

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